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Supporting Self-management: Development and Evaluation of a Digital Resource for Adults with Asthma

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Thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy to the University of Glasgow

General Practice & Primary Care
The School of Medical, Veterinary & Life Sciences
Institute of Health & Wellbeing

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Abstract

The problem
Around 300 million people worldwide have asthma and prevalence is increasing. Support for optimal self-management can be effective in improving a range of outcomes and is cost effective, but is underutilised as a treatment strategy. Supporting optimum self-management using digital technology shows promise, but how best to do this is not clear.

Aim
The purpose of this project was to explore the potential role of a digital intervention in promoting optimum self-management in adults with asthma.

Methods
Following the MRC Guidance on the Development and Evaluation of Complex Interventions which advocates using theory, evidence, user testing and appropriate modelling and piloting, this project had 3 phases. Phase 1: Examination of the literature to inform phases 2 and 3, using systematic review methods and focussed literature searching. Phase 2: Developing the Living Well with Asthma website. A prototype (paper-based) version of the website was developed iteratively with input from a multidisciplinary expert panel, empirical evidence from the literature (from phase 1), and potential end users via focus groups (adults with asthma and practice nurses). Implementation and behaviour change theories informed this process. The paper-based designs were converted to the website through an iterative user centred process (think aloud studies with adults with asthma). Participants considered contents, layout, and navigation. Development was agile using feedback from the think aloud sessions immediately to inform design and subsequent think aloud sessions. Phase 3: A pilot randomised controlled trial over 12 weeks to evaluate the feasibility of a Phase 3 trial of Living Well with Asthma to support self-management. Primary outcomes were 1) recruitment & retention; 2) website use; 3) Asthma Control Questionnaire (ACQ) score change from baseline; 4) Mini Asthma Quality of Life (AQLQ) score change from baseline. Secondary outcomes were patient activation, adherence, lung function, fractional exhaled nitric oxide (FeNO), generic quality of life measure (EQ-5D), medication use, prescribing and health services contacts.
Results

Phase 1: Demonstrated that while digital interventions show promise, with some evidence of effectiveness in certain outcomes, participants were poorly characterised, telling us little about the reach of these interventions. The interventions themselves were poorly described making drawing definitive conclusions about what worked and what did not impossible. Phase 2: The literature indicated that important aspects to cover in any self-management intervention (digital or not) included: asthma action plans, regular health professional review, trigger avoidance, psychological functioning, self-monitoring, inhaler technique, and goal setting. The website asked users to aim to be symptom free. Key behaviours targeted to achieve this include: optimising medication use (including inhaler technique); attending primary care asthma reviews; using asthma action plans; increasing physical activity levels; and stopping smoking. The website had 11 sections, plus email reminders, which promoted these behaviours. Feedback during think aloud studies was mainly positive with most changes focusing on clarification of language, order of pages and usability issues mainly relating to navigation difficulties. Phase 3: To achieve our recruitment target 5383 potential participants were invited, leading to 51 participants randomised (25 to intervention group). Age range 16-78 years; 75% female; 28% from most deprived quintile. Nineteen (76%) of the intervention group used the website for an average of 23 minutes. Non-significant improvements in favour of the intervention group observed in the ACQ score (-0.36; 95% confidence interval: -0.96, 0.23; p=0.225), and mini-AQLQ scores (0.38; -0.13, 0.89; p=0.136). A significant improvement was observed in the activity limitation domain of the mini-AQLQ (0.60; 0.05 to 1.15; p = 0.034). Secondary outcomes showed increased patient activation and reduced reliance on reliever medication. There was no significant difference in the remaining secondary outcomes. There were no adverse events.

Conclusion

Living Well with Asthma has been shown to be acceptable to potential end users, and has potential for effectiveness. This intervention merits further development, and subsequent evaluation in a Phase III full scale RCT.
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Acknowledgement

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I have also had notable support from several others. Without Kathryn Saunderson’s help with recruitment and trial visits I would not have got this far. Andrew Ramsey and Marilynn McGee Lennon gave expert help developing the website. Professor Lucy Yardley and Professor Mike Thomas provided invaluable input during the development of the website and I am delighted that the intervention featured in this thesis is going to be further developed under their direction. I would like to thank all who work in General Practice & Primary Care for their guidance, encouragement and help folding patient information leaflets in the days before the Christmas break. Much appreciated. In particular, I would like to thank the other occupants of room 303 (Katie Gallacher, Bhautesh Jani and David Blane) for their encouragement, advice and biscuits, Anna Black for our productive weekend writing sessions, and Michelle McKelvie, Chere Beaumont, Linda Easton and Jane Goodfellow for their practical help.

I thank the study participants, and the GP practices we recruited from. Without their participation, this project would not have been possible.

Last, but certainly not least some words about the support from my family, I would like to express my absolute gratitude to my husband Brian McGill, who married me 12 days into the start of this project. Had he known what it entailed he may not have turned up on the day. Thankfully he did, and we now have two beautiful girls, who I hope are still too young to realise how much of my time this PhD has taken up. Brian has risen to the challenge of being a stay at home dad, allowing me to dedicate the time and effort required to finish the project work and write this thesis. I would also like to thank my mum Jean Morrison for her many trips down to visit us and help with the girls, giving Brian and myself some much needed support.
Author’s Declaration

I am the sole author of this thesis, and was responsible for leading all aspects of the research as Chief Investigator except when I was on maternity leave (October 2011 to February 2012, and March 2015 to September 2015) when Professor Frances Mair took over this role.

The contents of the website pages were based on input from the expert panel (Professor Frances S Mair, Professor Sally Wyke, Professor Neil C Thomson, Professor Mike Thomas, Professor Lucy Yardley, and Dr Marilyn McGee Lennon), and the Asthma UK website with their permission. I drafted the text for a given section and incorporated comments as appropriate. Andrew Ramsay converted initial draft website pages onto LifeGuide software and generated the underlying logic to allow the website to function as planned. Either Andrew or I amended these pages based on feedback from think aloud studies, and further input from the expert panel.

I undertook all recruitment to the focus groups and think aloud studies. I was supported in recruitment to the main trial, which involved searching GP databases and generating letters, by Dr Kathryn Saunderson, and by Janice Reid, Yvonne McIlvenna and Tracy Ibbotson from the Scottish Primary Care Recruitment Network.

I oversaw recruitment of all participants and performed the role of trial manager except when on maternity leave when Dr Kathryn Saunderson took my place. The Robertson Centre for Biostatistics (RCB) who were responsible for database development and data entry. I undertook all analysis with support from Dr Alex McConnachie and Dr Caroline Haig from the RCB. I interpreted data with input from the expert panel.
Publications & Presentations

Publications arising from this project


Publications related to this project


**Morrison D., Mair FS., Yardley L., Kirby S., Thomas M.: Living with asthma and chronic obstructive airways disease: using technology to support self-management – an overview. Chronic Respiratory Disease 2016, In Press.**


Selected presentations arising from this project

**Morrison D., Wyke S., McConnachie A., Saunderson K., Thomson NC., Mair FS.: Lessons learned about asthma self-management from a pilot randomised controlled trial of a digital intervention. RCGP Annual Conference: 2015; Glasgow: (Poster Presentation, Prize winner).**


**D Morrison, S Wyke, NC Thomson, FS. Mair. The challenges of developing a relevant and practical online asthma resource. International Society of Quality in Healthcare (ISQua) Conference, Edinburgh, October 2013. (Oral Presentation)**

**D Morrison, E Cameron, G Braganza, N Thomson, R Chaudhuri, F Mair. Understanding recruitment challenges in Randomised Controlled Trials (RCTs) in primary care: findings from two asthma trials. SAPC Annual Scientific Meeting, July 2011. (Poster Presentation).**
### Abbreviations

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<th>Abbreviation</th>
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<tr>
<td>AA</td>
<td>African American</td>
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<tr>
<td>AAP</td>
<td>Asthma Action Plans</td>
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<tr>
<td>ACQ</td>
<td>Asthma Control Questionnaire</td>
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<tr>
<td>AE</td>
<td>Adverse Event</td>
</tr>
<tr>
<td>AMSTAR</td>
<td>A Measurement Tool to Assess Systematic Reviews</td>
</tr>
<tr>
<td>AQLQ</td>
<td>Asthma quality of life questionnaire</td>
</tr>
<tr>
<td>ATS/ERS</td>
<td>American Thoracic Society/ European Respiratory Society</td>
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<tr>
<td>BCT</td>
<td>Behaviour Change Technique</td>
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<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>BTS</td>
<td>British Thoracic Society</td>
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<tr>
<td>CI</td>
<td>Confidence Interval/ Chief Investigator</td>
</tr>
<tr>
<td>CTIMP</td>
<td>Clinical Trial Investigational Medicinal Product</td>
</tr>
<tr>
<td>CTU</td>
<td>Clinical Trials Unit</td>
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<tr>
<td>EQ-5D</td>
<td>Euroqol-5D</td>
</tr>
<tr>
<td>FeNO</td>
<td>Fractional Exhaled Nitric Oxide</td>
</tr>
<tr>
<td>FEV₁</td>
<td>Forced expiratory volume in 1 second</td>
</tr>
<tr>
<td>FG</td>
<td>Focus Group</td>
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<tr>
<td>FVC</td>
<td>Forced Vital Capacity</td>
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<tr>
<td>GINA</td>
<td>Global Initiative for Asthma</td>
</tr>
<tr>
<td>GP</td>
<td>General Practitioner</td>
</tr>
<tr>
<td>ICS</td>
<td>Inhaled Corticosteroids</td>
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<tr>
<td>IQR</td>
<td>Interquartile Range</td>
</tr>
<tr>
<td>ISRCTN</td>
<td>International Standard Randomised Controlled Trial Number</td>
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<tr>
<td>LOE</td>
<td>Languages other than English</td>
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<tr>
<td>MID</td>
<td>Minimal Important Difference</td>
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<tr>
<td>MMAS</td>
<td>Morisky Medication Adherence Scale</td>
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<tr>
<td>MRC</td>
<td>Medical Research Council</td>
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<tr>
<td>n/a</td>
<td>not available</td>
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<tr>
<td>NICE</td>
<td>National Institute of Clinical Excellence</td>
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<tr>
<td>NPT</td>
<td>Normalisation Process Theory</td>
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<td>NRAD</td>
<td>National Review of Asthma Deaths</td>
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<tr>
<td>PAM</td>
<td>Patient Activation Measure</td>
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<tr>
<td>PEF</td>
<td>Peak Expiratory Flow</td>
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<tr>
<td>PETS</td>
<td>Problems of Experienced Therapy Scale</td>
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<tr>
<td>PRISMA</td>
<td>Preferred Reporting Items for Systematic Reviews and Meta-Analyses</td>
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<td>QOF</td>
<td>Quality and Outcomes Framework</td>
</tr>
<tr>
<td>QOL</td>
<td>Quality of Life</td>
</tr>
<tr>
<td>R&amp;D</td>
<td>Research &amp; Development</td>
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<tr>
<td>RAISIN</td>
<td>Randomized Trial of an Asthma Internet Self-Management Intervention</td>
</tr>
<tr>
<td>RCB</td>
<td>Robertson Centre for Biostatistics</td>
</tr>
<tr>
<td>RCP 3Q</td>
<td>Royal College of Physicians 3 Questions</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomized Controlled Trial</td>
</tr>
<tr>
<td>RE-AIM</td>
<td>Reach, Efficacy, Adoption, Implementation, Maintenance</td>
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<tr>
<td>REC</td>
<td>Research Ethics Committee</td>
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<tr>
<td>RQ</td>
<td>Research Question</td>
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<tr>
<td>SAE</td>
<td>Serious Adverse Event</td>
</tr>
<tr>
<td>SAR</td>
<td>Serious Adverse Reaction</td>
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<tr>
<td>SD</td>
<td>Standard Deviation</td>
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<tr>
<td>SIGN</td>
<td>Scottish Intercollegiate Guidelines Network</td>
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<tr>
<td>SIMD</td>
<td>Scottish Index of Multiple Deprivation</td>
</tr>
<tr>
<td>SMS</td>
<td>short message services</td>
</tr>
<tr>
<td>SPCRN</td>
<td>Scottish Primary Care Research Network</td>
</tr>
<tr>
<td>SUSAR</td>
<td>Suspected Unexpected Serious Adverse Reaction</td>
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<tr>
<td>TA</td>
<td>Think aloud</td>
</tr>
<tr>
<td>TMG</td>
<td>Trial Management Group</td>
</tr>
<tr>
<td>VAS</td>
<td>Visual Analogue Scale</td>
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<tr>
<td>YHEC</td>
<td>York Economic Health Consortium</td>
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## Glossary

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tr>
<td><strong>Asthma control</strong></td>
<td>The extent to which manifestations of asthma are reduced or removed by treatment. This can vary.</td>
</tr>
<tr>
<td><strong>Asthma exacerbation</strong></td>
<td>Episodic worsening of asthma symptoms that are troublesome to patients, and that prompt a need for a change in treatment.</td>
</tr>
<tr>
<td><strong>Asthma severity</strong></td>
<td>The difficulty in controlling asthma with treatment. For example even with excellent adherence to available therapies control of symptoms remains difficult.</td>
</tr>
<tr>
<td><strong>Behaviour change theory</strong></td>
<td>Behaviour change theories are sets of statements or principles devised to explain why behaviours change, and that can be scientifically tested.</td>
</tr>
<tr>
<td><strong>Co-morbidity</strong></td>
<td>The presence of one or more long-term conditions in addition to an index condition</td>
</tr>
<tr>
<td><strong>Digital interventions</strong></td>
<td>Interventions delivered via the internet or non-internet means such as via text messaging, or using automated interactive voice response systems for example.</td>
</tr>
<tr>
<td><strong>eHealth</strong></td>
<td>An emerging field in the intersection of medical informatics, public health and business, referring to health services and information delivered or enhanced through the Internet and related technologies.</td>
</tr>
<tr>
<td><strong>Feasibility study</strong></td>
<td>Used to estimate important parameters that are needed to design a main study, such as ease of recruitment, standard deviations of outcome measures, and follow up rates.</td>
</tr>
<tr>
<td><strong>Framework</strong></td>
<td>A basic structure underlying a system, concept, or text.</td>
</tr>
<tr>
<td><strong>Framework analysis</strong></td>
<td>A type of qualitative analysis involving the use of a framework to sift, chart and sort data.</td>
</tr>
<tr>
<td><strong>Grade A recommendation</strong></td>
<td>A recommendation which has best available evidence to back it up e.g. at least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results. (Studies rated as 1+ or 1++ have either a low, or very low risk of bias). Definition from SIGN guidelines.</td>
</tr>
<tr>
<td><strong>Interactive intervention</strong></td>
<td>The intervention provides feedback autonomously and therefore delivers the intervention, at least in part, independently of any health professional, and communicates using any of a variety of methods such as on screen, email or text.</td>
</tr>
<tr>
<td><strong>Metareview</strong></td>
<td>A systematic review of systematic reviews.</td>
</tr>
<tr>
<td><strong>mHealth</strong></td>
<td>Health care supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices.” <a href="http://www.who.int/goe/publications/goe_mhealth_web.pdf">http://www.who.int/goe/publications/goe_mhealth_web.pdf</a> pg 6</td>
</tr>
<tr>
<td><strong>Normalisation Process Theory</strong></td>
<td>A middle range sociological theory that can be used to understand the processes involved in the implementation and embedding of a set of tasks.</td>
</tr>
<tr>
<td><strong>Pilot Trial</strong></td>
<td>A version of the main study that is run in miniature to test whether the components of the main study can all work together, and can work alongside existing practices.</td>
</tr>
<tr>
<td><strong>Self management support</strong></td>
<td>Giving people living with long-term conditions the tools, skills and support they need to improve their own wellbeing. It encourages them to find out more about their condition and learn new skills and tools to help them manage their own health better. (Definition adapted from <a href="http://www.selfmanagementuk.org">www.selfmanagementuk.org</a>).</td>
</tr>
<tr>
<td><strong>Self-efficacy</strong></td>
<td>Belief in one's ability to succeed in specific situations or accomplish a task.</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
</tr>
<tr>
<td>---------------------------</td>
<td>---------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Self-monitoring</td>
<td>Part of effective self-management in asthma and requires the patient to</td>
</tr>
<tr>
<td></td>
<td>monitor changes in their own clinical condition either using symptoms or</td>
</tr>
<tr>
<td></td>
<td>peak flow readings and respond to them appropriately.</td>
</tr>
<tr>
<td>Taxonomy</td>
<td>An ordered arrangement / list of groups or categories.</td>
</tr>
<tr>
<td>Telemedicine/telehealth</td>
<td>The delivery of health care from a distance.</td>
</tr>
<tr>
<td>Thematic analysis</td>
<td>A type of qualitative analysis that involves pinpointing, examining, and</td>
</tr>
<tr>
<td></td>
<td>recording patterns (or &quot;themes&quot;) within data</td>
</tr>
</tbody>
</table>
Chapter 1: Introduction & Background

1.1 Introduction

Asthma is a chronic relapsing condition which is associated with considerable morbidity and mortality [1, 2]. There are effective treatment options for asthma mainly using inhaled medications [3]. Mostly these treatments have to be taken regularly, even when the person is well, and adjusted accordingly when the person becomes less well [4]. As with many other chronic diseases, the availability of effective pharmacological treatments alone does not lead to better outcomes [5]. Improving self-management behaviours, primarily taking medication regularly and as prescribed, is an effective strategy for improving a range of asthma outcomes [6] and is recommended in asthma management guidelines both in the UK and worldwide [4, 7]. However, how best to support self-management is not clear [8]. What is clear however, is that as a treatment strategy, self-management support is not offered enough by health professionals, or utilised enough by those with the potential to benefit, and this is where the management of asthma is considered to be failing most [5, 9, 10]. This project aimed to help address these failings by developing and then investigating the role of a digital intervention to support self-management in adults with asthma.

1.2 Research motivation

The project came about through some hands-on experience in the field of asthma research and a fortuitous meeting in Oxford between one of my supervisors (Frances Mair) and a health psychology professor (Lucy Yardley) whose team were developing a software product called LifeGuide. This software allowed health professionals without a background in computer programming to develop websites both to provide information and to support health behaviour change.

My asthma research experience was gained during a one-year academic fellow post I commenced in August 2010. I worked with a team evaluating azithromycin in adults with asthma in a randomised controlled trial (RCT), and my main role was helping with recruitment. This involved phoning patients who had shown
interest in the study to review whether they met the inclusion / exclusion criteria. As a General Practitioner (GP), I am used to speaking to people with either a new diagnosis of asthma, or those experiencing an exacerbation. However, I rarely converse with those in-between: people who drift along with bothersome symptoms not bad enough to seek help for, but bad enough to significantly impact on day to day life, and I was surprised to realise that the majority of those I was talking to fell into this category. What was more surprising to me was how many of them did not take their preventer inhalers, this being the norm rather than the exception. The reason was virtually always ‘because I don’t really need them’. This was despite just spelling out for me in detail the symptoms they were experiencing and the effect it was having on their life. The discrepancy between people with asthmas’ assessment of their own control, and objective measures, I now know is well documented in the literature [11], however hearing it time and time again really made an impact on me as I had not been aware of this as such an issue previously. The people I was speaking to could all experience fewer symptoms if they took their prescribed medication - so why was this not happening, and what could I do to help? This realisation, combined with knowledge of the existence of LifeGuide software, led to the idea of developing a resource which targeted this group of people with a view to supporting self-management through adherence to prescribed medication and thus to improving asthma. A proposal for funding was drafted in conjunction with my four supervisors, and successfully submitted to the Chief Scientist Office. I was awarded funding for a 3-year fellowship to allow me to undertake the project, with the aim of achieving a PhD.

1.3 eHealth: Definitions & the role of the Internet

1.3.1 Introduction

I am going to briefly discuss eHealth and related terminology used in this thesis, and address concerns about the ‘digital divide’ which is often the first criticism levied at researchers working in this area. After this, I will describe my aims, research questions and provide the structure of this thesis to facilitate the reader in understanding how my planned project work was developed to meet each of my research questions.
1.3.2 eHealth definitions

The term eHealth is wide-ranging and comparatively generic, and was initially defined in 2001 by Gunther Eysenbach as follows [12]:

“e-health is an emerging field in the intersection of medical informatics, public health and business, referring to health services and information delivered or enhanced through the Internet and related technologies. In a broader sense, the term characterizes not only a technical development, but also a state-of-mind, a way of thinking, an attitude, and a commitment for networked, global thinking, to improve health care locally, regionally, and worldwide by using information and communication technology.”

A later systematic review from 2005 found 51 unique definitions of eHealth [13], of which Eysenbach’s was one of them. I value Eysenbach’s appreciation of the bigger picture, the fact that the development of eHealth represents not just a different mode of delivery for an intervention or a service but a completely new way of thinking. How ubiquitous the Internet has become over these last 14 years could barely have been predicted, yet I think this definition is still relevant, and with the development of smartphones, wearable technologies, and even ‘smart houses’ it can still be considered an emerging field.

Other related terms which appear in the literature include telemedicine and telehealth which broadly describe the delivery of health care from a distance. Initially eHealth interventions were alternative modes of delivering health professional led interventions, but as technology has become more sophisticated, interventions are increasingly being developed which can function without health professional input: the computer itself delivering the intervention. Terms such as web-based, online, Internet-based, digital, and computerised are often used interchangeably, although can mean different things in different contexts. In this thesis, I use the term digital when looking to include interventions delivered via internet and non-internet means such as with short message services (SMS), or using automated interactive voice response systems. Internet and web-based are interchangeable and refer to the fact that an internet connection is required (fixed or wireless) to at least download or use the intervention either on a computer, tablet or smartphone. I use the term interactive to represent the idea that a computer provides feedback and therefore delivers the intervention, at least in part, independently of any health
professional, and communicates using any of the methods above (e.g. SMS).

Another related term showing increasing prominence in the literature is ‘mHealth’, which is a component of eHealth. It has been defined as:

“medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices.”


Within this thesis, I use the overarching term eHealth.

Clarity in the terminology used has been lacking in the literature, although increasing calls for improved descriptions will hopefully have some impact [8, 14, 15], as will the increased uptake of the ehealth consort statement [16].

1.3.3 Does the digital divide still exist?

In short, the answer is undoubtedly yes, but is it the same issue it was 10 years ago? The answer is almost certainly no. By their nature, online interventions are only available to people who have access to the Internet, raising concerns that those without the Internet are at a disadvantage [17]. There are two hurdles to consider when thinking about physical access to the Internet. The first is the infrastructure, and both the Scottish and UK governments appear committed to improving this through various strategies such as increasing the availability of superfast broadband to 95% of the UK by 2017 [18]. The next hurdle is at an individual level – can a given person access the Internet? Again, the answer increasingly is yes. As of last year (2014) 84% of households in the UK had access to the Internet, up year on year since 2006 when it was only 57% [19]. Concerns about older populations not having access are increasingly unfounded with the percentage of adults aged 65+ years using a computer daily jumping from 6% in 2006 to 43% in 2014 as shown in Figure 1.1 [20].
As well as traditional means of accessing the Internet via a desktop or laptop in the home, alternative routes are increasingly available such as mobile phones, tablets or smart TVs. The number of adults accessing the Internet via mobile phone has more than doubled between 2010 to 2014 to 58%, and the increase in the over 65s age group has increased over 5 fold from just 2% in 2010 to 11% in 2014 [21]. So although the over 65 year age group continues to lag behind, growth of Internet and computer use in this age group far exceeds that of the younger populations suggesting it may only be a matter of time before the age related digital divide ceases to exist.

The other main concern regarding the increase in health services delivered online relates to concern that it will be contributing to health inequalities given that those who live in deprived areas have less access to internet than those from more affluent areas [22]. However again there is evidence of this gap narrowing, with the gap between the percentage of households with internet in the most deprived areas versus the rest of Scotland falling from 25% in 2007 to 15% in 2012, data shown in Figure 1.2 [22].
In addition, improving access via public libraries and community centres is a key recommendation within the Digital Scotland report from the Royal Society of Edinburgh [17]. There is evidence of its importance as an option particularly in areas with high deprivation and lower Internet adoption such as Glasgow, UK [23]. It is also worth mentioning that Internet access is already available through most computer game consoles, and increasingly now through digital television. In the UK, smart TVs make up 45% of the market share, a 60% increase year on year [24] and there is evidence that technology utilising digital TV is already being developed in the field of health and social care [25, 26].

Overall, the physical barriers to Internet access appear to be lessening year on year. However there are further considerations about access in terms of health literacy, or particularly ‘ehealth’ literacy [27]. Poor health literacy in general is a global concern, and a recognised barrier to improved health outcomes, being associated with reduced knowledge, increased morbidity and increased use of health services [28].
Good eHealth literacy requires not only traditional literacy, but also health literacy and computer literacy [27]. However, it is false to assume that information or interventions delivered over the Internet are automatically harder for those with poorer literacy to access when compared to more traditional means. For example poor aural literacy (listening skills) contributes to poor asthma outcomes [29] so Internet interventions with scope to provide written and oral content alongside each other may work to actually overcome literacy barriers. Similarly, concern that reduced health literacy is associated with less use of online resources is refuted in this study where teenagers with low health literacy used the Internet just as much as those with high health literacy [30].

The links between deprivation and lower health literacy are long recognised, however there are exciting new developments challenging this assumption that eHealth materials are less accessible to deprived populations. A recently published smoking cessation intervention was found to be only effective in those with low socioeconomic status (SES). What was particularly interesting was that user testing of the intervention was done exclusively with smokers with low SES, in response to previous work that had suggested Internet support only worked in those with high SES [31]. This result was not in isolation, but backs up earlier work in this area by the same research group [32]. What this suggests is that if the target audience is truly involved at the planning and development level these barriers are surmountable.

1.3.4 eHealth summary

This data demonstrates that concern about the digital divide, while important to be aware of, should not in any way hinder ongoing development of interventions delivered by this medium, so long as consideration towards delivery via multiple mediums such as traditional computer, portable devices and smart TVs for example, and the specific needs of the target audiences are attended to.
1.4 Overview of this project work

1.4.1 Aims and research questions of project

The overarching aim of this project was to explore the potential role of a digital intervention in promoting optimum asthma self-management to adults with asthma.

The project was testing the hypothesis that an intervention co-designed with key stakeholders, developed to be evidence-based and theory-informed, is likely to be acceptable to the target end users, and likely to merit progression to a full scale randomised controlled trial (RCT) of efficacy.

I therefore generated four overarching research questions (RQs) which, if addressed, would allow me to meet my aim above. This process of generating the research questions is fully described in Chapter 3.

RQ 1 - What is known about the effects of online tools to promote self-management of asthma and what helps or hinders their utilisation by patients?

RQ 2 - What are the barriers and facilitators to the uptake and utilisation of a web-based self-management tool from the perspective of adults with asthma, and primary care nurses who undertake asthma reviews?

RQ 3 - Can evidence from the literature (asthma management and theory) and input from potential end users, be successfully incorporated into an intervention to promote self-management?

RQ 4 - What would be the feasibility of undertaking a randomised controlled trial of the digital intervention, and how would such a website be used by adults with asthma. What would be the effect on symptom score and quality of life measures be?

Basing the project work on these four RQs naturally led to the project having three distinct, but related, stages. These are described in the next section.
1.4.2 Outline of project stages

Stage 1 is the initial examination of the literature. For this I undertook a metareview (systematic review of systematic reviews) of digital self-management interventions. The aim of this stage was to answer research question 1, and inform the subsequent stage of the project: developing the website (stage 2).

Stage 2 describes four separate work packages which illustrate how I used multiple sources to feed into the development of the website, and answers research questions 2 and 3. These sources included focus groups and think aloud studies to incorporate potential end users’ input, evidence from the literature, including relevant theory, and incorporating the experience of an expert panel. The development of the website was not a linear process, but with various work packages occurring alongside each other. By the end of second stage I had developed a working interactive website called ‘Living Well with Asthma’.

Stage 3 was the work of evaluating the Living Well with Asthma website in a pilot RCT, with additional feasibility outcomes. This aims to answer research question 4. I conducted a 12 week parallel group RCT with target sample size of 50. Participants were randomised either to the intervention group where they were given access to the website, or the comparison group which received usual care.

1.5 Overview of the thesis

This thesis takes the form of 9 chapters, listed in Table 1.1.
Table 1.1 Overview of Chapters

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Overview</th>
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<tbody>
<tr>
<td>1</td>
<td>Introduction</td>
</tr>
<tr>
<td>2</td>
<td>Background</td>
</tr>
<tr>
<td>3</td>
<td>Methodological considerations</td>
</tr>
<tr>
<td>4</td>
<td>Metareview of digital asthma self-management interventions</td>
</tr>
<tr>
<td>5</td>
<td>Developing the ‘Living Well with Asthma’ self-management website</td>
</tr>
<tr>
<td>6</td>
<td>Evaluating the ‘Living Well with Asthma’ self-management website</td>
</tr>
<tr>
<td>7</td>
<td>Comparison with similar intervention evaluations</td>
</tr>
<tr>
<td>8</td>
<td>Discussion</td>
</tr>
<tr>
<td>9</td>
<td>Conclusion</td>
</tr>
</tbody>
</table>

Chapter 1 is this brief introductory chapter. It provides a context to the study, and my research motivations. I introduce the topic of eHealth, and address concerns about the ‘digital divide’. I describe my aims and objectives, and the motivation for the research. Lastly, I illustrate the format of the project work, and then within this final section, the structure of the thesis itself.

Chapter 2 provides firstly a background overview of the diagnosis, epidemiology, and pharmacological management of asthma. It then provides an up to date literature review to investigate barriers, identified by adults with asthma, to taking asthma medication as prescribed, and finally it describes what interventions which aim to improve self-management might contain, and reflects on how these features might work in a digital intervention.

Chapter 3 is where I discuss methodological issues arising from this body of work. In particular, I explain the rationale for mixed methods studies and provide an introduction to the use of theory when developing and evaluating complex interventions, and the importance of incorporating user preferences. I describe how each of my four research questions were developed, and why specific methods were chosen to answer them.

Chapter 4 provides the methods, results and discussion of the meta-review of digital asthma interventions. This corresponds to stage 1 of my project.

Chapter 5 describes the methods, results and discussion of the development work undertaken to make the Living Well with Asthma website. An abridged description of this phase was published by BMC Medical Informatics and Decision
Making in July 2015, and is found in appendix 2. This chapter corresponds to stage 2 of my project.

Chapter 6 describes the evaluation of Living Well with Asthma website: A pilot Randomised Controlled Trial of an Asthma Internet Self-Management Intervention, the RAISIN study. This chapter describes the methods, results and discussion from this evaluation stage of the project. The protocol for this RCT is published in Trials Journal [33] (and included as appendix 1), and results are published in BMJ Open (and included as appendix 3). This chapter corresponds to stage 3 of my project.

Chapter 7 is an updated review of the literature to find RCTs of comparable interventions in order to compare my results with that available.

Chapter 8 is a discussion which brings the results of all 3 project stages together (Chapters 4, 5 and 6). I discuss how well I have answered my research questions and discusses the overall conclusions in the context of the current literature. I will describe the strengths and weaknesses of the project overall.

Chapter 9 concludes this thesis. Here I provide overall conclusions, consideration for future directions and discuss implications for practice and policy.
Chapter 2: Background

2 Introduction

This aim of this chapter is to present the rationale for the content of the intervention developed later in this thesis (and described in Chapter 5). It has three sections. First, it provides a background overview of the diagnosis, epidemiology, and pharmacological management of asthma. Second, it provides an up to date literature review to investigate barriers, identified by adults with asthma, to taking asthma medication as prescribed. Third, it describes what interventions which aim to improve self-management might contain, and reflect on how these features might work in a digital intervention, such as that being developed here.

The chapter does not include a review of published evaluations of digital self-management interventions as that literature review is covered separately in chapter 7, to allow for comparison with the intervention developed in chapter 5 and the evaluated in primary 6.

2.2 Asthma

2.2.1 Introduction

An overview of how asthma is diagnosed, its epidemiology and accepted pharmacological management is essential to understand some of the challenges faced by those with an interest in improving asthma outcomes. This is provided in this section, drawing on published guidelines/reports [1, 4, 7, 34] and Cochrane Reviews [6, 35].

2.2.2 Definition and diagnosis

Providing a definition of asthma is not as straightforward as it is with many other diseases. The Global Initiative for Asthma (GINA) [7] provides one definition:
“Asthma is a heterogeneous disease, usually characterised by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation.”

The recent British guidelines [4], on the other hand, shy away from providing a definition at all, going as far as to say that the absence of a ‘gold standard definition’ makes providing evidence based recommendations for diagnosis impossible.

A third position was suggested in draft NICE guidelines initially available for consultation in early in 2015. These draft documents, viewed in July 2015, suggested that NICE would recommend much more extensive investigations in people with suspected asthma with specific cut offs for a ‘positive’ or ‘negative’ test result to indicate the presence, or not, of asthma [36]. These tests include a measure of lung function (spirometry), of inflammation (fractional exhaled nitric oxide, FENO) and of airway hypersensitivity (bronchial challenge). Concerns raised in response to these draft documents was such that the publication date is now ‘To be confirmed’ to allow primary care based feasibility work to be undertaken to better understand the impact of these new guidelines.

While there is lack of consensus over the definition of asthma, there is to date an agreement that the diagnosis is essentially a clinical one, based on the typical symptoms such as those described in the definition above.

People with a diagnosis of asthma are often characterised by stating on which ‘step’ of the British Thoracic Society (BTS) asthma treatment ladder (Figure 2.1) they are on [4]. The ladder offers primary care practitioners guidance on how to ‘step up’ treatment for adults with asthma until either they achieve acceptable control, or they reach step 5, at which point referral to secondary care is indicated, if not already undertaken.
This summary of the stepwise management of asthma is reproduced from SIGN British Guideline on the management of asthma 141 (pg 9) by kind permission of the Scottish Intercollegiate Guidelines Network [4].

It is worth taking a moment to clarify terminology used when describing someone’s asthma, in particular the terms control, severity and exacerbation. The American Thoracic Society/European Respiratory Society (ATS/ERS) convened a task force to do just that, and I summarise their definitions in Table 2.1 [34].
Table 2.1 Definitions of terms used in asthma

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
<th>Further explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>'the extent to which manifestations of asthma are reduced or removed by treatment'</td>
<td>Two areas to consider when assessing control: 1) current level of control (measured e.g. by symptoms, quality of life) 2) risk of future adverse events including exacerbations but also loss of control</td>
</tr>
<tr>
<td>severity</td>
<td>'the difficulty in controlling asthma with treatment'</td>
<td>Severe asthma is where control is difficult to achieve with exclusion of modifiable factors such as non-adherence, smoking. E.g. even on appropriate treatment control is still inadequate.</td>
</tr>
<tr>
<td>exacerbation</td>
<td>'episodes that are troublesome to patients, and that prompt a need for a change in treatment'</td>
<td>• Mild exacerbations: not defined, as considered part of the normal variation in control • Moderate exacerbations: a deterioration in symptoms and/or lung function for ≥2 days requiring increased reliever use, not warranting oral steroids • Severe exacerbations: oral steroids required</td>
</tr>
</tbody>
</table>

These distinctions are important in order to both standardise clinical endpoints within trials, and to emphasise that asthma control is not the same as severity. Just because someone is considered to have mild asthma does not mean they are not at risk of loss of control and exacerbations; almost 10% of those in the National Review of Asthma Deaths (NRAD) were classified as having mild asthma when they died [1].

2.2.3 Epidemiology

Asthma is common, affecting an estimated 300 million people world-wide [37], and 5-10% of populations in developed countries. Although one report suggests Scotland has the highest prevalence of asthma symptoms in the world (18.4%, compared to England 15.1%, USA 10.9%, and Germany 6.9%), it also ranks in the lowest quarter for case fatalities [37]. This may suggest that Scotland manages acute exacerbations to a high standard, but the day to day management of symptoms less well.

Worldwide, the number of disability-adjusted life years lost due to asthma has been estimated at 15 million per year, similar to that for diabetes [37]. More women than men have asthma [2], and the reason for this is not known. While around half of children labelled as asthma ‘grow out of it’ by adulthood, adults with it are rarely ‘cured’. Previously it has been thought that asthma mostly starts in childhood, however within the National Review of Asthma Deaths the
median age of onset of asthma in those who died was 37 years, with 69% diagnosed after 15 years of age [1]. Recent epidemiological studies suggest that individuals with asthma have more comorbidity than expected, further adding to the challenges of managing an already complex condition [38].

### 2.2.4 Pharmacological management

Asthma is a disease with variable symptoms and consequently a variable need for medication. This is demonstrated visually in the stepwise management by the presence of an arrow going both ways (Figure 2.1). When an individuals’ asthma deteriorates or improves over the longer term and the treatment changes in order to manage these symptoms this is termed ‘stepping up’ and ‘stepping down’. As Figure 2.1 demonstrates, short acting bronchodilators (relievers), followed by the addition of inhaled corticosteroids (ICS) or ‘preventers’ remains the mainstay of asthma management. Those who remain uncontrolled on these medications are offered increased ICS doses and/or the addition of further medications until ideally good control is achieved.

Transient changes to medication during exacerbations include increasing frequency of reliever inhaler, and if severe the addition of a short course of oral steroids. The benefits of doubling, or possibly even quadrupling, ICS during exacerbations has yet to be proven [35]. If there are multiple exacerbations a year, or there is a longer history of uncontrolled symptoms, this would be an indication to add or increase regular medications e.g. step up the treatment ladder.

### 2.2.5 Treatment goals in asthma

The GINA guidelines list the goals for successful management of asthma [7]:

1. Good control of symptoms;
2. Maintain normal activity levels;
3. Minimise future risk of exacerbations, fixed airflow limitation, and medication side effects.
Chapter 2 Background

These goals are not widely achieved and care of patients with asthma is often considered suboptimal [37, 39, 40]. One underlying explanation for this is a consistent discrepancy in perceived levels of asthma control: patients overestimate their control, and underestimate symptoms. Put another way people with asthma endure greater symptoms and lifestyle limitations than necessary [2, 41].

Although the goal of the GINA guidelines is to ‘maintain normal activities’ what this actually means is not clear. If an individual stops playing football regularly because she experiences wheeze and shortness of breath, it becomes normal for her not to play football. Then from that person’s point of view they are maintaining their normal activities, not recognising they have modified what is normal for them to reduce likelihood of them experiencing asthma symptoms.

This is the challenge with improving asthma outcomes - helping people with asthma to recognise that their symptoms are modifiable with the right treatments. This topic is explored in the following section on non-adherence.

2.3 Literature review of barriers to adherence

2.3.1 Research question

What are the barriers to taking asthma medication as prescribed identified by adults with asthma (limited to treatments aimed at mild to moderate asthma e.g. step 1-4 on the BTS ladder, excluding newer immunotherapies aimed at those with severe disease)?

2.3.2 Methods

2.3.2.1 Search Strategy

MEDLINE, EMBASE and Health and Psychosocial Instruments were searched using a search strategy developed in a previous review I had undertaken which had also aimed to capture qualitative articles [8]. It involved finding articles from 3 main search areas:

1. asthma
2. adherence to medications
3. qualitative methods/patient experience

Asthma: asthma has features which make it distinct from other chronic diseases such as the use of inhalers rather than tablets, and the variable nature of the illness burden. Given the volume of articles on adherence, it seemed reasonable to narrow this down on articles focusing on asthma, in particular those which featured adults with asthma. Therefore I limited my search to articles which mentioned the term asthma* in the abstract.

Adherence: the literature on adherence is vast and it has its own MeSH subject heading: medication adherence. This was used as a starting point, with the addition of any article with adher* or nonadher* or non-adher* in the title or abstract. The terms compliance or comply was also used.

Qualitative: I used terms such as experience* qualitative* and exploded terms such as interview, using the ‘or’ function to try and capture any paper which included this type of language in its title or abstract.

These were limited further by excluding articles with terms such as ped* or paed* in their titles to remove articles featuring children from the search strategy. The remaining articles were limited to ‘human’ and English language. This full search strategy is shown below.
I included articles which provided insights into why people with asthma didn’t take their medications as prescribed: either featuring adults with asthma, or reporting others’ views on this topic such as health professionals’ opinions. A similar process for selecting qualitative papers has been used elsewhere [42].

### 2.3.2.2 Quality appraisal

A quality appraisal instrument was used to allow me to describe the quality of the included articles in this review. Unlike with quantitative reviews there is some debate about whether quality appraisal is appropriate, with some believing that each piece of qualitative research is important in its own right and cannot be compared to another [43], whereas others [44, 45], myself included, feel that it is a useful step when synthesising qualitative articles, providing additional information to base conclusions on. There is no consensus about the best

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**Table 2.2 Search strategy for literature review**

<table>
<thead>
<tr>
<th>Search strategy for literature review</th>
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<tbody>
<tr>
<td>1. (patient$ adj3 (experience$ or attitude$ or view$1 or satisfaction$)).ti,ab.</td>
</tr>
<tr>
<td>2. qualitative research.mp. [mp=ti, ab, ot, nm, hw, kf, px, rx, ui, an, tn, dm, mf, dv, kw, ac, sh, de, md, ip, vo, pg, sd, jn, pb, yr, ar, bs, bt, cf, dp, ja, pa, so]</td>
</tr>
<tr>
<td>3. exp Interviews as Topic/</td>
</tr>
<tr>
<td>4. qualitative.ti,ab.</td>
</tr>
<tr>
<td>5. locus group.mp. [mp=ti, ab, ot, nm, hw, kf, px, rx, ui, an, tn, dm, mf, dv, kw, ac, sh, de, md, ip, vo, pg, sd, jn, pb, yr, ar, bs, bt, cf, dp, ja, pa, so]</td>
</tr>
<tr>
<td>6. asthma*.ti,ab.</td>
</tr>
<tr>
<td>7. (non-adher* or nonadher* or adher*).ti,ab.</td>
</tr>
<tr>
<td>8. medication adherence/</td>
</tr>
<tr>
<td>9. ((compliance or comply) adj3 (medic* or treat* or therap* or inhale*)).ti,ab.</td>
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<tr>
<td>10. 7 or 8 or 9</td>
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<tr>
<td>11. interview*.ti,ab.</td>
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<tr>
<td>12. 1 or 2 or 3 or 4 or 5 or 11</td>
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<tr>
<td>13. 12 not (rct or randomi* or pilot*).ti.</td>
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<tr>
<td>14. 6 and 10 and 13</td>
</tr>
<tr>
<td>15. limit 14 to english language</td>
</tr>
<tr>
<td>16. limit 15 to human</td>
</tr>
<tr>
<td>17. limit 16 to yr=&quot;2005 -Current&quot;</td>
</tr>
<tr>
<td>18. 17 not (ped* or paed* or child*).ti.</td>
</tr>
<tr>
<td>19. remove duplicates from 18 (total 278 articles)</td>
</tr>
<tr>
<td>20. from 19 keep 2,4,6,10,14-15,27,36,48-49,61,66,72,76,82,87,94,99,102,111,115,118-</td>
</tr>
<tr>
<td>119,127,132,135,142,154,173,195,199,206,240,247</td>
</tr>
</tbody>
</table>

**Key:**

- / indicates a subject heading
- exp indicates an exploded subject heading
- * truncation symbol
- adj3 words must appear with 3 words of each other
- .ti,ab. searches are restricted to the title and abstract fields
strategy for undertaking quality appraisal, and I elected to use a questionnaire developed by my colleague Katie Gallacher [45], that I have experience of personally using in a systematic review of treatment burden in stroke [46] where I felt it worked well. The tool itself is based on published guidance on systematically reviewing qualitative studies from respected qualitative researchers [47]. It consists of eleven questions, each considering an aspect such as rigour and generalisability. There is no scoring or ‘pass mark’; the results are used to inform the discussion only.

2.3.2.3 Analysis

Each article was read and information about participants, study type and strengths and limitations were noted. The results and discussions were read closely and any text which could be construed as describing a barrier was extracted. These individual barriers were examined, and related barriers grouped to develop categories of barriers to adherence. A narrative summary was then provided for each category.

2.3.3 Results

2.3.3.1 Search results

Running the search described above found 418 articles, 288 after de-duplication. This number could not be refined further using electronic searching without risking the loss of useful articles, so was manually reviewed. This led to 34 articles being reviewed at full paper, and 10 articles being included.

2.3.3.2 Quality appraisal

The results of the quality appraisal are summarised in Table 2.2, and specific areas of strengths or weakness identified are commented on in Table 2.4. Most studies were well conducted when using this appraisal tool. The pattern suggests that newer studies are more methodologically sound, with the only 2 studies with less than <10 positive responses being older (2008 [48], and 2005 [49]). The main areas for concern was the lack of information about the researchers own influence on the data, and the absence of declaration of conflicts of interest.
2.3.3.3 Description of included papers

Full papers included are described in Table 2.4 below which lists author, date, aim, methods participants, barriers identified and strengths and weaknesses.

Nine of the papers featured people with asthma, and one featured general practitioners as participants and one paper featured health professionals and patients. Eight of the nine articles featuring participants with asthma provided a mean age, and in 6 of these 8 articles the mean age was >42 years. The other two articles had particularly targeted younger adults [50, 51]. Six were set in North America, 2 in Australia, and one each in Sweden and the UK. Three articles employed focus group methodology with the remaining using semi-structured interviews.
Table 2.3 Quality appraisal summary

<table>
<thead>
<tr>
<th>Question adapted from [46, 47]</th>
<th>Article number as per Table 2.4</th>
</tr>
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<tbody>
<tr>
<td>Does the research, as reported, illuminate the subjective meaning, actions, and context of those being researched?</td>
<td><img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /></td>
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<tr>
<td>Are subjective perceptions and experiences treated as knowledge in their own right?</td>
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<tr>
<td>Is there evidence of the adaption and responsiveness of the research design during the course of the study?</td>
<td><img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /></td>
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<td>Does the sample produce the type of knowledge necessary to understand the structures and processes within which the individuals or situations are located?</td>
<td><img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /></td>
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<td>Is the description provided detailed enough to allow the researcher or reader to interpret the meaning and context of what is being researched?</td>
<td><img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /></td>
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<td>Are any different sources of knowledge about the same issue compared and contrasted?</td>
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<td>Has the researcher rendered transparent the processes by which data have been collected, analyzed, and presented?</td>
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<td>Has the researcher made clear their own possible influence on the data?</td>
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<tr>
<td>Is it clear how the research moves from a description of the data, through quotation or examples, to an analysis and interpretation of the meaning and significance of it?</td>
<td><img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /></td>
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<tr>
<td>Are claims being made for the generalisability of the findings to either other bodies of knowledge or to other populations or groups reasonable?</td>
<td><img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /></td>
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<tr>
<td>Is there the absence of any other aspect of the study that may affect the quality e.g. conflict of interest?</td>
<td><img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /></td>
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● answer to question is yes
<table>
<thead>
<tr>
<th>No</th>
<th>Author(s)</th>
<th>Date</th>
<th>Aim of paper</th>
<th>Type of Study/information</th>
<th>Barriers identified in study</th>
<th>Strengths and weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>George M Keddem S Barg FK Green S Glanz K</td>
<td>2015</td>
<td>Identify urban adults’ perceptions of facilitators and barriers to asthma control, including the role of self-care, medications, environmental trigger remediation, and primary care</td>
<td>Methods: Semi-structured open-ended qualitative interviews. Modified grounded theory approach. Participants: (n = 35) purposive sample from previous research study to include participants from range of areas in West Philadelphia, USA. Age: mean 55 years; Female: 71%. SES: 40% Medicaid; 17 % completed high school. Ethnicity: 94% AA; 6% white Other: 71% uncontrolled;</td>
<td>Prefer alternative therapies/dislike medications in general Perceived overprescribing Difficulty with routine/forgetting Doubts about efficacy Poor patient/HCP relationship</td>
<td>+ Demographics fully described including age, gender, race, education level, Insurance and BMI. - Despite purposive sampling stratifying for gender most participants were female, black and overweight. COI information not provided</td>
</tr>
<tr>
<td>2</td>
<td>Pelaez S Bacon SL Aulls MW Lacoste G Lavoie KL</td>
<td>2014</td>
<td>Examine the perspectives of asthma patients, physicians and allied health professionals regarding adherence to asthma medication.</td>
<td>Methods: 6 focus groups. Inductive coding, constant comparison. Participants: patients (n= 13); respiratory physicians/ allied health professionals (n=25) purposive sample enrolled from a university affiliated general hospital in Montreal Canada. Age: mean 52.5 yrs; Female: 69% (patients) SES: n/a; Ethnicity: n/a Other: 62% ACQ&gt;1; 80% reported good adherence; mean asthma duration 30 years (range3-75)</td>
<td>Inhaler difficulties Difficulty with routine/forgetting Cost/access to care Doubt/denial of diagnosis Perceived overprescribing Societal acceptability Side-effects</td>
<td>+ Participants well described. Triangulation of data between different sources. Purposive sample. - Recruited from single university affiliated institution and most patients well controlled/good adherence.</td>
</tr>
<tr>
<td>3</td>
<td>McDonald VM Higgins I Gibson PG</td>
<td>2013</td>
<td>Explore older peoples’ experiences of asthma or COPD with reference to their journey in the healthcare system.</td>
<td>Methods: Qualitative interview. Line-by-line analysis of interviews performed, coded for common themes. Participants: (n = 21), enrolled from respiratory ambulatory care clinics in New South Wales, Australia Age: mean 68.6 years (range 59-82); Female: 71% SES: n/a Ethnicity: n/a Other: mean time since diagnosis 30 yrs</td>
<td>Poor patient/HCP relationship Difficulty with routine/forgetting Doubts about efficacy Perceived overprescribing Lack of information</td>
<td>+ Participants well described. - Only discussed themes they perceived as being novel. Consecutive sampling</td>
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<td>No</td>
<td>Author(s)</td>
<td>Date</td>
<td>Aim of paper</td>
<td>Type of Study/information</td>
<td>Barriers identified in study</td>
<td>Strengths and weaknesses</td>
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<td>4</td>
<td>Axelsson M Lotvall J Lundgren J Brink E</td>
<td>2011</td>
<td>Elucidate adherence reasoning in relation to asthma medication.</td>
<td>Methods: Qualitative interview via telephone. Purposive sampling (mix of adherence scores). Analysis informed by Grounded Theory methods. Participants: (n = 18) enrolled from previous study in Sweden Age: 22 ±1 years; Female: 72% SES: 56% current students; 61% university educated. Ethnicity: n/a Other: mostly well controlled; 11% ED visit and 11% oral steroids in preceding 12months</td>
<td>• Poor patient/HCP relationship • Doubt/denial of diagnosis</td>
<td>+ Participants fully described including education level, income, occupation 10/18 students - Atypical narrow sample, all 22 years old, mostly students, only discusses this briefly whereas aim of study broad.</td>
</tr>
<tr>
<td>5</td>
<td>Baptist AP Deol BB Reddy RC Nelson B Clark NM</td>
<td>2010</td>
<td>Elucidate common challenges in asthma management faced by older adults across the demographic spectrum, including both community dwelling elders and those in residential facilities.</td>
<td>Methods: 6 focus groups with participants&gt;65 years. Semi structured questions. 3 coders independently identified categories line by line and generated themes. Participants: (n = 46) enrolled from university based health systems, one in affluent area one in deprived area in Michigan, USA Age: mean 72.6 years; Female: 85% SES: mixed Ethnicity: 50% white; 43.5% AA; 6.5% other. Other: 57% reported no social support to help with asthma; majority uncontrolled asthma.</td>
<td>• Lack of information • Side-effects • Cost/access to care • Difficulty with routine/forgetting • Prefer alternative therapies/dislike medications in general • Absence of good social support</td>
<td>+ Purposively recruited from affluent and deprived areas. - Excluded those with dual COPD asthma diagnosis smokers or ex-smokers with &gt; 20 pack year, potentially missing difficulties of managing both conditions together.</td>
</tr>
<tr>
<td>No</td>
<td>Author (s)</td>
<td>Date</td>
<td>Aim of paper</td>
<td>Type of Study/information</td>
<td>Barriers identified in study</td>
<td>Strengths and weaknesses</td>
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<tr>
<td>6</td>
<td>Naimi DR Freedman TG Ginsburg KR Bogen D Rand CS Apter AJ</td>
<td>2009</td>
<td>Describe adherence to preventive asthma medications and explore relevant beliefs and attitudes in older urban adolescents.</td>
<td>Methods: Two semi-structured interviews 1 month apart. Analysed using grounded theory structure Participants: (n = 40) Philadelphia, USA; Age: 15-21 years; Female: 48%. SES: Low income urban area; 28% Medicaid insured Ethnicity: 75% AA; 28% White (could choose more than one) Other: median adherence of 43% of doses; 60% previously hospitalised.</td>
<td>• Perceived overprescribing • Difficulty with routine/forgetting • Inhaler difficulties • Side-effects • Absence of good social support • Societal acceptability</td>
<td>+ Participants well described. Used health belief model to inform analysis. - Had normal inhaler swapped for one which monitored adherence so not entirely normal practice, but not an intervention study so included here.</td>
</tr>
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<td>7</td>
<td>Choi TN Westermann H Sayles W Mancuso CA Charlson ME</td>
<td>2008</td>
<td>Identify patients' beliefs about asthma medications and to assess these beliefs according patient and asthma characteristics, including asthma severity and patient-reported medication adherence.</td>
<td>Methods: Interviews, 3 researchers independently coded quotes and agreed on categories and overarching themes Participants: (n = 52), enrolled from scheduled office visits with physicians in New York City, USA Age: mean 43 years; Female: 87% SES: 42% college graduates Ethnicity: 31% Caucasian, 42% AA, 21% Hispanic Other: mean MMAS adherence score 1.6 (very low). Mean asthma duration 26 years.</td>
<td>• Difficulty with routine/forgetting • Inhaler difficulties • Prefer alternative therapies/dislike medications in general • Side-effects • Doubts about efficacy • Perceived overprescribing</td>
<td>+ Participants well described. - Convenience sample. Secondary analysis of qualitative study about physical activity and asthma, so participants not specifically asked about medication adherence.</td>
</tr>
<tr>
<td>8</td>
<td>Gamble J Fitzsimons D Lynes D Heaney LG</td>
<td>2007</td>
<td>Explore the experiences of patients with difficult asthma, who take corticosteroid therapy, and provide insight into why some patients comply with therapy, whilst others do not.</td>
<td>Methods: Non-structured interviews. Analytical framework to guide analysis Participants: (n = 10) Enrolled from secondary care clinic in Belfast, UK Age: mean 44 (range 25-58); Female: 70% SES: n/a Ethnicity: n/a Other: at least 1 oral steroid course in preceding year.</td>
<td>• Side-effects • Doubts about efficacy • Lack of information • Prefer alternative therapies/dislike medications in general • Societal acceptability • Difficulty with routine/forgetting • Poor patient/HCP relationship</td>
<td>+ Purposive sample, continued until data saturation. - Participants not well described. Recruited from single clinic. No COI information provided.</td>
</tr>
<tr>
<td>No</td>
<td>Author(s)</td>
<td>Date</td>
<td>Aim of paper</td>
<td>Type of Study/information</td>
<td>Barriers identified in study</td>
<td>Strengths and weaknesses</td>
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| 9  | Tumiel-                    | 2006  | Describe how perceptions and experiences of patients with asthma or caregivers affect asthma management in a Puerto Rican community in Buffalo, NY.                                                  | Methods: 2 focus groups, semi structure interview style. Grounded theory approach to analysis. Participants: (n = 22) invited through flyers/word of mouth from Puerto Rican community in New York, USA Age: n/a; Female: n/a SES: n/a Other: n/a                                                                 | • Cost/access to care  
• Lack of information  
• Side-effects  
• Doubts about efficacy                                                                 | + Multilingual researchers used to minimise risk of losing data during translation.  
- Little description of participants. COI information not provided                                                                                     |
| 10 | Goeman DP                  | 2005  | Ascertain what GP’s priorities are for achieving optimal outcomes in people with asthma, and the barriers they face in delivering this care.                                                                  | Methods: 6 discussion groups were asked “What do you think is needed to achieve best outcomes for asthma care?” Nominal Group Technique Consensus was reached on the emerging themes by 4 researchers Participants: GPs (n = 49): 34 city/suburban; 15 rural. Australia. | • Lack of information  
• Cost/access to care                                                                                                                        | + Purposive recruitment from inner city, urban and suburban areas.  
- Did not discuss own strengths and limitations. Minimal description of analysis methods.                                                   |

AA  African American; COI  conflict of interest; GP  general practitioner; HCP  health care professional; MMAS  Morisky Medication Adherence scale; SES  socioeconomic status.
2.3.3.4 Adherence barriers established

A total of 12 categories of barriers were identified by people with asthma. Health care professionals also identified 8 of these 12 barriers, and did not identify any barriers not already described by those with asthma. The four barriers that were not identified by health care professionals are marked with a double asterisk **. The 12 categories of barriers are:

1. Doubts about, or denial of, diagnosis of asthma [51, 58]
2. Perceived over prescribing of asthma medications ** [48, 50, 52, 54, 58]
3. Doubts about efficacy of asthma medications ** [48, 52, 54, 56, 57]
4. Concern about side-effects, including fear of addiction [48, 50, 55-58]
5. General preference for ‘natural’ therapies, and dislike of taking medications in general [48, 52, 55, 56]
6. Lack of ‘correct’ information about symptoms and treatment options [49, 54-57]
7. Absence of trusting patient/health professional relationship ** [51, 52, 54, 56]
8. Absence of good social or family support [50, 55]
9. Practical difficulties of incorporating regular medications into daily routines/forgetting ** [48, 50, 52, 54-56, 58]
10. Inhaler difficulties e.g. not user friendly, ensuring physical access to them [48, 50, 58]
11. Societal acceptability of taking inhaler medications [50, 56, 58]
12. Cost/physical access to care and medicines [49, 55, 57, 58]

Each is discussed in turn.

1) Doubts about, or denial of, diagnosis of asthma [51, 58].

Rationale behind these concerns centred round the fact that many of the symptoms of asthma such as cough or shortness of breath were often experienced by other people without asthma leading participants to question whether they really did have an illness at all. Both studies reporting this barrier had participants described as having well controlled asthma.
2) Perceived over prescribing of asthma medications ** [48, 50, 52, 54, 58]

In several studies this barrier was linked to doubts about diagnosis fuelling a belief that medications prescribed weren’t necessary. However many others did not question their diagnosis, but did question whether they really needed all their prescribed medications, particularly that daily medication was required. Many participants preferred to only take their medications when they were particularly symptomatic, feeling that tolerating mild symptoms is preferable to a medicine. A USA based study evaluating barriers between controlled and uncontrolled participants [52] found that those with uncontrolled asthma were more likely to report perceived over prescribing. What this study did not do was investigate adherence, so it is impossible to know whether these individuals were uncontrolled because they were not taking their medications, which seems more likely, or whether they were uncontrolled despite taking their inhalers.

3) Doubts about efficacy of asthma medications ** [48, 52, 54, 56, 57]

Five individual studies with varying participant demographics reported this barrier. In some cases the demographics themselves may contributed to this perception, such as in George et al [52] most participants were obese, a factor which is known to contribute to reduced response to treatment, and this group were also reported as having uncontrolled asthma. In general terms they may have been correct to have felt their medications were not working. In Gamble et al [56] patients were more likely to have severe asthma, and in Choi et al very low adherence rates were noted [48], possibly fuelling their perceptions that asthma medications weren’t not working. Despite experiencing asthma for decades two further studies still identified this barrier [48, 54].

4) Concern about side-effects, including fear of addiction [48, 50, 55-58]

This barrier was one of the mostly commonly identified barriers to adherence. Occasionally established side effects were the concern, such as oral thrush [57] or jitteriness following salbutamol [48], but often side-effects not normally attributed to inhaled steroids were of concern such as vomiting, bone pain or weight gain [57, 58]. Occasionally there was confusion where side effects of oral steroids such as osteoporosis, weight gain, mood swings and cataracts were being attributed to inhaled steroids [55].
Chapter 2 Background

5) Dislike of taking medications/ general preference for ‘natural’ therapies [48, 52, 55, 56]

This was also a common theme and was often coupled with a concern about side effects. Use of natural therapies (i.e. not medications) was found in both uncontrolled and controlled populations by George et al [52], but interestingly those with controlled asthma tended to use more evidence based alternative strategies such as stress relief, breathing exercises, and social support. However, those with uncontrolled asthma reported using the evidence based strategies but they also used a range of strategies without an evidence base, such as cold compresses, or buying houseplants to enrich household oxygen levels. A second study explored this barrier in detail and found that some individuals used potentially harmful strategies such as licking salt, and most worrying was that while most participants reported using alternative strategies, no one had discussed them with their health care professionals, citing that they wouldn’t be interested [55].

6) Lack of ‘correct’ information about symptoms and treatment options [49, 54-57]

There were several findings that contributed to this category. Firstly, patients reported not having access to information about treatment options such as asthma action plans [55] or information about new treatments despite reporting a desire for such information [54]. This was consistent with the study of GPs where Goeman et al found that few GPs promoted action plan use, despite the evidence of benefit [49]. Older participants commented that health care professionals often presumed the patients knew everything already and therefore were felt to not volunteer further information [56]. The remaining study reported examples of misinformation (e.g. nebulisers are for cleaning lungs) [57].

7) Absence of trusting patient/health professional relationship ** [51, 52, 54, 56]

Recurrent reports of participants feeling ‘not heard or recognised’ contributed to this theme [54], and the importance of targeting this barrier was explored by George et al [52] who established that those with uncontrolled asthma reported poorer relationships with their health care professionals than those with controlled asthma. This poorer relationship seemed to link in with perceived
overprescribing of medications, particularly contributing to poor adherence. Other participants felt that only seeing a health care professional infrequently left them unable to build up a trusting relationship and were therefore unable to have confidence in the advice they received [51]. Those with more severe asthma felt they knew more than their GPs did about their condition [56].

8) Absence of good social or family support [50, 55]
The two studies which highlighted this barrier were interestingly studies which focused on older adults > 65 years or older teenagers aged 15-21 years and it was at these extremes of age that the absence of good support was noted as a barrier. Older adults as features in Baptist et al [55] were often managing their condition alone. They described being unable to rely on family or spouses as, if present, the family/spouses had health problems deemed more severe than the asthma participants. The younger age group [50] described instances where difficult social circumstances affected their ability to take their medication as prescribed, such as one teenage boy describing a difficult relationship with his father which meant he often had to flee his house at short notice and stay elsewhere, usually leaving his medication behind.

9) Practical difficulties of incorporating regular medications into daily routines/forgetting ** [48, 50, 52, 54-56, 58]
This was one of the more commonly mentioned barriers across the studies, but not identified by health professionals. Participants of all ages reported this as a barrier with studies aimed at older teenagers [50] reporting that they simply forget to take them, especially when well. In contrast, the other study aimed at younger adults did not identify this barrier [51], but this latter study were mostly well educated students who had asthma most of their lives. One study aimed at older adults (mean age 72.6) reported that they wanted to take their medications regularly, but forgot, citing memory problems and polypharmacy as barriers this [55]. Gamble et al featured adults at the more severe end of the spectrum, of working age, and this group specifically reported a conflict for them between allocating time to take medications versus time to allocate to other demands on their time such as their family and home life, finding it difficult to prioritise their medication regimes [56]. Choi et al reported being disciplined about their regimes was burdensome, and this was considered the biggest drawback of their condition for these participants [48]. The remaining
articles mentioned simply forgetting inhalers, or being too busy to fit them in [52, 54]

10) **Inhaler difficulties e.g. not user friendly, ensuring physical access to them [48, 50, 58]**

Despite the participants featured in Pelaez et al’s study being generally well controlled and reporting good adherence, they specifically described inhalers as being difficult to use and a barrier to adherence [58], and participants in Choi et al reported that inhalers were bulky and difficult to carry around [48]. The study aimed at older adolescents [50] described a unique barrier here, in that this group frequently stayed at friends’ houses, often at short notice, and therefore were not able to take their preventer inhalers as they hadn’t anticipated not staying at home. The health professionals in Pelaez et al [58] also cited this barrier, both the physical aspects of the inhalers being difficult to use, but also the fact that a prescription was required to access them, and if a person could not access a health professional either due to location, time or financial reasons then they would go without their medicine. This concern about physically accessing a prescription and keeping their inhalers in date was also cited by participants in Choi [48].

11) **Perceived societal acceptability of taking inhaler medications [50, 55, 56, 58]**

This was a barrier common to younger and older participants, and also identified by health professionals [50, 58]. It was discussed in detail with participants in Gamble et al study [56] where participants felt that ‘having to use an inhaler in public was perceived as showing a fragility they preferred to disguise’.

12) **Cost/physical access to care and medicines [49, 55, 57, 58]**

Some participants from a Puerto Rican community in New York City described having to wait until their symptoms became severe enough to attend the emergency department, due to a lack of health insurance [57]. Participants in other studies described having to ration their medications due to costs [58] while health professionals from the same study also recognised that cost was a significant barrier to adherence. The GPs based in Australia also reported the same concerns [49].
2.3.4 Discussion of adherence literature

2.3.4.1 Summary of findings

This review of literature describing barriers to taking asthma medications included 10 individual articles. In general, these studies were methodologically sound. From these articles, I identified 12 different categories of barriers and have discussed each in turn. Discussing these barriers with adults with asthma would be the next step in terms of taking these forward and incorporating them into an online resource. This is described in Chapter 5.

2.3.4.2 Barriers identified by patients but NOT health care professionals

It would be worth giving further attention to the 4 barriers not identified by health professionals, as these would be important to address in a resource which is aiming to supplement a health professional review. The difficulty of remembering to take an inhaler and fitting it into daily routine was the most commonly identified barrier by patients, but was not identified by health professionals at all. This highlights a real learning point for health care professionals to recognise that following a treatment regime is just one of many priorities that an individual may have, and encouraging honest conversations about capacity might allow a more acceptable treatment regime to be agreed and ideally adhered too.

Another two, linked, barriers not mentioned by health care professionals were the perceived overprescribing and doubts about efficacy of asthma medications. Health care professionals are likely to be confident that they have made an appropriate diagnosis, and are prescribing the correct medication, but are clearly not conveying this confidence to patients. This leaves lingering doubts with patients which feed into poor adherence. Actively eliciting these doubts, if they exist, and addressing them is an essential step. Exploring this barrier with adults with asthma using qualitative methods would be essential to inform any asthma adherence intervention.

The final barrier not acknowledged by HCP is the importance of the relationship between HCPs and patients. Perhaps unsurprisingly health professionals did not question whether their relationship with patients impacted on levels of
adherence. Challenging this barrier in a resource would be difficult; it is largely HCP’s responsibility and the resource developed here is for people with asthma.

2.3.4.3 Area of conflict within articles.

Several studies highlighted the paradoxical findings they reported. Participants in Gamble et al [56] complained that they were not provided with the information they desired, and that health care professionals often assumed they knew everything already. However, they also felt frustrated that they seemed to know more about their own condition than their GPs did. Other examples were highlighted by Axelsson [51] referred to the same participants doubting their diagnosis, and being reluctant to take inhaled steroids regularly, but still reporting that they wouldn’t go anywhere without their reliever inhaler in case their symptoms flared. Resolving these areas of conflict for people with asthma would be worthwhile endeavour for such an intervention as that being developed here, but would be challenging. User testing to check responses to the content and ensure understanding would be essential, as there is clearly much scope for misinterpretation.

2.3.4.4 Comparison with existing literature

A comprehensive and well conducted synthesis of qualitative studies undertaken by Pound et al [59] provides a background to this subject. This synthesis included 4 asthma studies and a further 33 studies covering disease areas such as HIV, hypertension, mental health and gastrointestinal symptoms, and studies about medicines in general. This study aimed to understand ‘lay experiences of medicine taking’ and in doing so identified a range of barriers to adherence. Overall, they conclude:

“the main reason people do not take their medicines as prescribed is not because of failings in patients, doctors or systems, but because of concerns about the medicines themselves. On the whole, the findings point to considerable reluctance to take medicine and a preference to take as little as possible.”

My findings are very similar to Pound et al’s and serve to demonstrate that barriers identified in this older review are still relevant. Each barrier found in my review, was discussed, at least in broad terms, in Pound et al’s synthesis, but
Chapter 2 Background

not always directly attributed to the asthma studies, for example concerns about societal acceptance was discussed in terms of studies included participants with HIV or on medication for mental illness. There were no barriers in relation to asthma that my review missed, and there were two new specific issues identified in my literature review. These were the lack of ‘user friendly’ inhaler devices, and the specific barriers young people experience, especially those with poor social support. This suggests that while asthma may have slight differences in terms of inhalers rather than tablets, these differences are perhaps less important than I initially thought, and that barriers to adherence are generally universal to most chronic illnesses.

A more recent narrative review of research on non-adherence published in 2012 [60] provides a description of the problem, and suggests strategies for improving the situation using the Information-Motivation-Strategy model. Di Matteo concludes:

“Nonadherence is a complex problem and addressing it requires the efforts of both patients and clinicians, as well as all members of the healthcare team, and the individuals who are part of the patients’ everyday lives.”

Their findings emphasise in greater detail than Pound et al [59] the importance of good communications skills on the part of health professionals and how much impact a positive relationship can have on improving adherence. Their strategy can be simplified as actively eliciting barriers to patients taking their medications, and working with them to overcome these barriers.

My literature review, along with these two well conducted and comprehensive reviews provide a good understanding of the problem, and Di Matteo in particular suggests some ways that health professionals can support people to take their medicines as prescribed, within a consultation. However, evidence based strategies for implementing these strategies are lacking. Recent reviews of interventions to improve adherence have focussed on mobile health, or reminders (mainly short message service (SMS)). Tao et al [61] examined the use of reminders, and included four asthma studies. Three used SMS and one used a pager like device with audio-visual reminder (green light and beep). Overall, they found a small but statistically significant positive effect with the use of reminders, which was found to be larger when asthma alone was examined as a
subgroup. However they also noted that trials with smaller sample sizes had larger effect sizes, and that given three of the four asthma trials were small (<100 participants) this effect needs to be interpreted with caution. Similarly the three asthma studies also used additional self-management tools (information, advice, tailoring) so it is impossible to separate out the active ingredient. Their main conclusion was a call for more adequately powered good quality trials.

Given that non-adherence is so widespread it would be expected that it would be the focus of lots of good quality research, however a recent Cochrane review published in 2014 concluded the opposite [62]. This review evaluated 182 RCTs testing interventions to improve adherence, and only 17 were considered to be at low risk of bias. The authors lamented an ongoing issue of underpowered studies, which had not improved from their previous review in 2008, although how many of these were purposely so in the form of pilot studies is not clear. There were some positive findings however, and for long term treatments these included simplifying the dosing regimen, and a number of more complex strategies (including more detailed patient instruction, reminders, supervised self-monitoring, and rewards for success) appeared to be most successful. What is concerning here is that many of these ‘complex’ strategies that are shown to work in trial settings do not seem to translate well into real life settings. When I looked specifically at the 12 asthma trials, the findings are even less encouraging. Only two showed a benefit in adherence and clinical outcomes, with the remaining showing no difference. There is little to distinguish the two successful interventions from the remaining, other than they both had higher sample sizes (211 and 267). In their discussion, the authors recommend there should be at least sixty participants per group if there is to be any hope of distinguishing between treatment groups, a scenario that seems to rarely happen in trials to date.

2.3.4.5 Strengths and Weaknesses of literature review

Whilst the search strategy was provided, and comprehensive, and quality appraisal was undertaken the articles were screened only by one person. Including articles published only in 2005 or later could be seen as a limitation. However health care has changed considerably in the last decade; new inhalers
are available and information is much easier to obtain than ever before. I was specifically looking to use these barriers to inform the content of a website, therefore there was little to gain from capturing historical barriers which no longer apply to current health care scenarios.

### 2.3.5 Conclusion

This literature review shows the reasons for people not taking medications as prescribed are multifactorial, but that establishing what these barriers are is an essential starting point for any resource aiming to improve asthma outcomes. The barriers identified here are based on articles worldwide, and may not all be relevant to the target population of the resource being developed here. So while these barriers can directly inform the potential contents of a resource, exploring them with potential end users is essential to understand what is relevant to those who will ultimately be using this resource.

### 2.4 Self-management as a treatment strategy

#### 2.4.1 Introduction

In this remaining section, I explore what an intervention aiming to promote self-management might contain, and how these might translate to a digital intervention. Adherence has been explored in the preceding section and its influence on the contents of a self-management intervention is described fully in Chapter 5. This section will include other aspects of self-management: asthma action plans (AAPs); improving inhaler technique; trigger avoidance; exacerbation risk factors; goal setting; psychological functioning; self-monitoring; and finally a brief note about the health professional review itself.

This topic has been the subject of several Cochrane Systematic Reviews [6, 63-65] and is described in several published asthma guidelines [4, 7], therefore this background section mainly draws on these resources.

#### 2.4.2 What is self-management

Gibson et al’s Cochrane systematic review entitled ‘Self-management education and regular practitioner review for adults with asthma’ [6] was pivotal in
changing the focus of asthma guidelines. It included a good number of RCTs (36 in total evaluating: education \((n=36)\); self-monitoring \((n = 33)\); regular review \((n=24)\); and written action plan \((n = 18)\)). A preceding Cochrane review had already indicated that information alone was not sufficient to improve outcomes \([66]\), and the encouraging results from individual evaluations of ways to support self-management were hinting that supporting self-management had real potential to make a difference. This subsequent 2002 Cochrane review provided the robust evidence that guided self-management, as part of systematic planned care, incorporating the use of personal asthma action plans, was the best combination of ‘optimum self-management’. They reported that this ‘optimum’ self-management led to improvements in patient outcomes such as increases in knowledge, confidence and quality of life, as well as reductions in hospitalisations, emergency room visits, unscheduled visits to the doctor, and days off work or school \([6]\). It was particularly convincing that while individual types of self-management support (regular review, or using actions plans for example) often showed slight benefit, the real benefits came when all were present, hence the term ‘optimum self-management’. Gibson et al optimum self-management is summarised visually in Figure 2.2 \([6]\). This allowed the guidelines to provide evidence based advice that directly influenced policy here in the UK, for example when providing asthma self-management support was included in the GP contract in 2004.

**Figure 2.2 Optimum self-management**

- Receive self-management education (including how to self-monitor)
- Use a written action plan
- Attend regular health professional review
- Optimum self-management
The British Thoracic Society/Scottish Intercollegiate Guidelines Network (BTS/SIGN) Guideline on the Management of Asthma continues to stipulate the importance of promoting self-management, and reiterates throughout that a written asthma plan should be provided to everyone as part of the annual primary care asthma review [4]. The increased priority that the guidelines are placing on self-management is visible by reviewing the changes from the most recent guidelines in 2014, compared to the previous 2008 version. The chapter on self-management is now twice as long, and comes immediately after the diagnosis chapter, whereas in the 2008 guidelines it was half the size and was the last chapter - an afterthought. Support for self-management aims to improve outcomes in a number of ways: improved recognition of deteriorating symptoms, more appropriate responses to exacerbations, and finally improving adherence to medication [67]. Features of self-management support

2.4.2.1 Asthma action plans (AAPs)

AAPs are considered a crucial component of self-management and recent British guidelines make two grade A recommendation about their use [4]:

1. All people with asthma (and/or their parents or carers) should be offered self-management education, which should include a written personalised asthma action plan and be supported by regular professional review.
2. In adults, written personalised asthma action plans may be based on symptoms and/or peak flows: symptom-based plans are generally preferable for children.

Teaching individuals to recognise deterioration and act in a timely manner is a crucial step in reducing severe exacerbations, hospitalisation and potentially even asthma related deaths [1, 68], and AAPs are a written agreed plan for doing this. The importance of providing AAPs was a key message from the National Review of Asthma Deaths [1], as from the 195 deaths reviewed only 23% had a record of being provided with an AAP (from either primary or secondary care). Out of the patients who died who had not sought medical assistance during their final attack only 17% (11/33), had been provided with an AAP, compared to 36% of those who had sought help but died before it could be
administered (8/22), perhaps indicating that having an AAP increases the chances of an individual seeking more timely medical advice.

Despite their clear benefits AAPs are underused [1, 10, 69, 70], and a comprehensive systematic review tried to understand why [9]. They recognised two important mismatches: 1) content/design and 2) target audience. Firstly, they found that professionally provided, medically focussed, action plans often do not fit with patients'/ carers views of asthma, and do not incorporate patients’/carers’ experience. Secondly, they found that health professionals appeared to believe they were mainly useful for educated patients, with well controlled asthma, and patients felt that action plans were most appropriate in severe asthma or where care is being provided out with the usual set up (e.g. in school), and did not consider themselves as candidates for benefitting from their use.

The overall conclusion is that patients do not feel that action plans are relevant or useful to their own person circumstances. Tailoring of action plans to increase relevance should increase their worth to the individual [64, 68, 71]. However specific examples of how to achieve this are lacking in the literature, and the BTS guidelines simply state that use of personalisation of AAPs need to be considered within “the broader challenges of living with asthma” [4].

It is clear that Asthma UK have attempted to simplify and personalise their AAP within the limitations of a paper based template, and some of their changes are shown in Table 2.5.

<table>
<thead>
<tr>
<th>Table 2.5 Differences in Asthma UK AAPs 2011 to 2014</th>
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<tbody>
<tr>
<td><strong>2011 version</strong></td>
</tr>
<tr>
<td>Four different ‘zones’:</td>
</tr>
<tr>
<td>1. Your asthma is under control…</td>
</tr>
<tr>
<td>2. Your asthma is getting worse…</td>
</tr>
<tr>
<td>3. Your asthma is much more severe..</td>
</tr>
<tr>
<td>4. It is an emergency if…</td>
</tr>
<tr>
<td>‘Normal activities’</td>
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</table>

The impact on uptake and use of these readily available more personal AAPs will be difficult to assess. At present, they would still need to be printed and taken
to an asthma review to fill in with a health professional. It has been shown AAPs are likely to work best when agreed between an individual and a health professional they trust [64]. What is less clear is whether this ‘organic’ process of agreement of action plan ‘actions’ can be replicated successfully by a computer program without discussion between the health professional and the patient. Verbally agreeing specific actions in response to the presence or absence of specific symptoms or peak flow readings, while maintaining the level of personalisation that Ring et al recommend for patients to actually use them in real life may not be amenable to any computer generated algorithm [9]. Developing such a computer feature would be lengthy, time consuming, and require more piloting time than we could provide in this project, before being used by patients. An alternative option to improve access to asthma action plans could be providing a template that users could print out and discuss with their health professional. This would require to be supplemented with, behaviour change advice outlining the benefits of AAPs, promoting their ease of use, and encouraging a discussion between the patients and their health professionals.

2.4.2.2 Inhaler technique

Poor inhaler technique is the main reason for patients unintentionally not taking medications. It is known that poor inhaler technique contributes to poor asthma control, and this is compounded by an ever increasing array of inhalers [72, 73], with evidence that health professionals can be as confused as patients [73]. A further barrier to assessing and improving inhaler technique by health professionals is the difficulty in accessing placebo inhalers, and if the patients forget to bring their own, teaching inhaler technique becomes difficult.

As an option for overcoming the barrier of no placebo inhalers, videos have been shown to be an effective way of improving recall regarding correct inhaler use, and avoiding triggers, particularly so in those with limited literacy [74]. Improving inhaler technique clearly warrants inclusion in any intervention to promote self-management, digital or otherwise.
2.4.2.3 Trigger avoidance and predictors of exacerbations

When aiming to improve asthma control there are two areas to consider: 1) current clinical control (e.g. symptoms), and 2) future risk of exacerbation [34, 75]. With regard to assessing future risk, all of the following have been shown to be important contributors [75]:

1. history of previous exacerbation
2. poor asthma control
3. poor inhaler technique
4. a history of lower respiratory tract infection
5. non-adherence
6. presence of allergic rhinitis
7. gastro-oesophageal reflux disease
8. psychological dysfunction
9. smoking
10. obesity

Often individuals are aware of their own personal triggers such as animal dander. These predictors provide some guidance about topics to include in any self-management intervention, and raising awareness of an individual’s predictors of exacerbations, or loss of control, may be a suitable strategy.

2.4.2.4 Goal setting

Goal setting has been a component of successful interventions in asthma [76], and are undergoing further evaluation at present in a RCT [77]. Qualitative work in the area showed that goals relating to lifestyle (e.g. person, family, work) were far more meaningful to patients when compared to mediatory ones such as those relating specifically to asthma control [78]. The BTS/SIGN guidelines recognise the potential for goal setting when they state: ‘Brief simple education linked to patient goals increases acceptability to patients’. Incorporating goal setting into self-management interventions is one way to personalise the intervention ideally increasing engagement.

2.4.2.5 Psychological functioning

This topic has been summarised in a clinical review article by Thomas et al in 2011 [79]. In summary, they found that psychological dysfunction is more common in people with asthma than would be expected by chance alone, and
the relationship between impaired asthma control and quality of life and depression and anxiety appears to be independent of potentially confounding factors of age, socioeconomic status (SES), asthma severity etc. The presence of anxiety and depression are associated with worse outcomes, but effective treatment strategies are lacking. Since their review there is further evidence that this is an ongoing issue worldwide [80], but little progress in the way of guidance on management. The exception is work that Thomas et al are undertaking regarding the role of breathing exercises. These have been shown to improve patient reported outcomes and psychological measures such as anxiety states [81] and an intervention focusing on breathing exercises is currently being evaluated in a RCT ongoing at present [82].

In a similar vein, qualitative work shows that in order to allow a person with asthma to achieve as near normal activities as possible, family members need to be on board with the asthma management strategies [83]. In real life clinical practice many patients have little or no social support. Therefore establishing and acknowledging this isolation as an additional barrier to patients' practicing optimum self-management may allow for further personalising of action plan advice, and may modify what would be expected of a given patient.

Discussing the potential interplay between psychological functioning, family support and asthma outcomes should be part of a health professional review, particularly where uncontrolled asthma is detected, as it could be a contributory factor. Incorporating this aspect of asthma self-management into a digital intervention is likely to be challenging, other than highlighting it as an issue in the first place.

2.4.2.6 Self-monitoring

Self-monitoring is often considered an important aspect of self-management as it is felt that timely intervention in the face of deteriorating symptoms can avert progression to a severe exacerbation, and interventions with self-monitoring were more effective than interventions without [6, 84]. However, it is interesting to note that the latest BTS guidance has moved away from the term ‘self-monitoring’; only discussing ‘recognition of deteriorating symptoms’ instead.
This may seem surprising as the rationale behind promoting self-monitoring is convincing. An analysis of exacerbations (n = 425) within a large RCT of asthma treatments found that participants displayed evidence of deteriorating asthma control (a decline in PEF, increase in symptom scores or increase in reliever use) which initially occurred gradually for 5-7 days followed by a more rapid change over the 2-3 days before the exacerbation [85]. Other studies have found similar results [86].

However, it is harder to find evidence of any effective interventions showing sustained self-monitoring by participants [87], and there is a lack of clarity about why individuals rarely sustain self-monitoring. One theory is that patients are poor at recognising deterioration in symptoms in the first place, and therefore are then unable to act appropriately, a non-intentional lack of self-monitoring [9]. Alternatively, patients do recognise deterioration in symptoms but alter their medication inappropriately due to lack of awareness of what their deteriorating symptoms mean [88]. These explanations are consistent with the literature which shows that those with asthma overestimate their control, and underestimate their symptoms [2, 89]. This is the case even in trial settings when presumed exemplary education on self-monitoring is provided [90].

Either way, it seems that regular self-monitoring as I understand it at present, is not well used by individuals with asthma generally. Variations that could make it more acceptable include reducing the recommended frequency, e.g. weekly monitoring may be enough in those with well or partly controlled asthma, and that this could safely become less frequent once good control is achieved [91]. More imaginative strategies have been employed in recent studies where a sensor on a reliever inhaler detects increasing use, communicating via Bluetooth to a smartphone or similar device the evidence of deteriorating control indicated by increasing reliever use with encouraging preliminary results [92]. It seems plausible that this type of ‘passive’ monitoring may be far more acceptable to patients.

Overall the evidence that self-monitoring is effective at improving outcomes is clear, but how best to facilitate it is not, and until methods more acceptable to patients become available it is difficult to know how best to increase uptake.
2.4.2.7 Health professional review

At present in the UK, regular review means a face to face, pre-arranged appointment. However not all patients are willing or able to attend, particularly given most people perceive themselves as being well, so attendance remains suboptimal. In the National Review of Asthma Deaths published in 2014, only 57% of those who died had evidence of a routine asthma review in the preceding year. Being flexible about how to provide the regular review appears helpful, with evidence that telephone reviews are safe and effective [93], and whether there is a role for asthma reviews to be undertaken within a digital intervention remains to be seen.

In terms of contact with health professionals between reviews a proportion of those with asthma would value having email access to health professionals [41], and with more practices offering online messaging this may be increasingly feasible even in the short term. There are risks associated with this as it is not feasible for practice staff to regularly monitor online messaging so boundaries about what type of queries could be raised in this way would need to be clearly outlined. As with other health areas promotion of resources available in the third sector could alleviate this gap, for example Asthma UK provide a daily telephone service to speak to a trained asthma nurse Monday - Friday during working hours, which could answer general queries and concerns an individual may have.

Clearly there is scope for improving the uptake of asthma reviews, and whether a digital intervention should aim to complement health professional review, or could in part replace it, is not yet clear from the literature.

2.4.3 Implications for future digital self-management interventions

Taking these findings into account can provide a picture of what could be considered for inclusion in a digital intervention to promote self-management. There are some items where there is little debate about rationale for inclusion, with strong evidence to recommend their inclusion. These would include inhaler technique, review of triggers and risk factors for exacerbations, and promoting awareness of the interplay between psychological state and asthma outcomes.
There is strong evidence that AAPs work, and their use be promoted, but there is little evidence suggesting the feasibility of taking this a step further with a digital intervention generating one automatically. Promoting daily self-monitoring may not be helpful if patients are not going to do it anyway, therefore using AAPs which are based on signs and symptoms of deteriorating asthma control may be the most feasible solution, at least until methods of ‘passive’ monitoring are more readily available. There is some evidence that objective methods of assessing control such as structured questionnaires may overcome the issue of patients downplaying their symptoms, and this was used somewhat successfully in one large RCT of a comprehensive digital self-management intervention [94]. Finally, the role of the health professional review requires consideration in the development of an online intervention.

There is strong evidence for a regular health professional review, but no evidence as yet that a digital intervention could replace it. Where there are varying degrees of evidence behind different components, these need to be discussed with potential end users in order to understand more clearly how these features could be successfully implemented into a digital intervention, as is reported in chapter 5.

2.5 Chapter conclusion

The aim of this chapter was to allow the reader to gain an understanding of the status of asthma and its management, and develop an understanding of what optimum self-management involves and how it may potentially be supported by a digital intervention. Barriers to adherence were explored in a review of the literature, in order to inform the contents of the intervention as described in Chapter 5. The next step is to consider formally the processes involved in developing and subsequently evaluating a digital intervention, and the next chapter looks at these methodological issues.
Chapter 3: Methodological Considerations

3.1 Chapter overview

This chapter introduces the terminology used when discussing the philosophical and methodological origins of research, and describes how my understanding of this has changed during this fellowship. I will then explain how I generated the four research questions outlined in chapter 1, followed by a discussion of the methodological considerations encountered while deciding on the most appropriate methods to answer each research question.

Silverman describes methodology as ‘a general approach to studying research topics’, and method as ‘specific research technique’ [95]. This chapter primarily concerns itself with the former, while the actual methods used in this project are described in their relevant chapters (meta-review methods in chapter 4, website development methods in chapter 5, and randomised controlled trial (RCT) methods in Chapter 6).

3.2 Introduction

It is clear the research questions outlined in the first chapter demand a mix of methodologies to adequately answer them. Historically there has been a viewpoint that qualitative and quantitative methods are so different in their philosophical and methodological origins that using both together cannot be recommended. However, due to an increasing appreciation of the multiple ways in which we need to understand factors which impact on health and wellbeing, using a mix of methods is increasingly being advocated [96].

While my research experience prior to embarking on this fellowship was primarily of using quantitative methods, I thought I had a good appreciation of why mixed methods were not only acceptable, but also positively advocated. Therefore, as a novice researcher, as I was then, I was surprised that it was still considered important to justify the use of mixed methods. It seemed to be common sense that different methods would provide different knowledge:
gathering knowledge from as wide a range of sources as possible could only be beneficial.

However, as I have explored the philosophical origins of research during this fellowship, I realise my understanding of qualitative methods at the start was actually very narrow. I saw the role of qualitative research as primarily a way of explaining or validating quantitative results. During this fellowship I have gained a greater understanding of the different research paradigms that researchers work across, strengths and weaknesses and the potential role each can have. My stance is now firmly that when combining qualitative and quantitative methods, they should be seen as equal and distinct from each other; the choice of method should be based on the research question being answered.

A rationale for using a mix of methods in this PhD has been provided by Ritchie et al [97] as follows:

“Each of the two research approaches is seen as providing a distinctive kind of evidence and, used together, they can offer a powerful resource to inform and illuminate policy or practice” p40.

It is clearer to me now why researchers want to use mixed methods, and funders may look favourably upon proposals incorporating them [96]. The challenge with this project was finding the right methods to provide the best data to answer each of the research questions.

3.3 Background

Silverman (2001) argues that a given methodology should not be considered right or wrong, but rather more or less useful for a given research question [95]. Methodology is the way we go about discovering knowledge in a systematic way. Appropriate methodological choices are considered to be driven by one’s ontological and epistemological beliefs. Simply put, ontology refers to beliefs about the nature of reality, and epistemology refers to beliefs about the nature of knowledge, and how it can be acquired [98]. I will discuss these further below.
I had previously been aware of two dominant research strategies: quantitative and qualitative. A simplified description being that quantitative methods are involved with measuring, when qualitative are not [99]. However, I now realise that these research strategies align to differing ontological and epistemological principles, and here are more correctly discussed in terms of the two dominant research paradigms within social research: positivism and interpretivism.

During my reading on this topic, I became aware that researchers used similar terms in slightly different ways. For example Bryman uses the term ‘objectivism’ to describe an ontological orientation [99] (pg 36), however Ormston uses the term to describe an epistemological stance [98] page 6. In response to this variation in terminology used, I constructed a table which links terms to the paradigm they are mostly aligned with (see Figure 3.1 below): broadly describing positivism and interpretivism.

**Figure 3.1 Terms aligned to positivism and interpretivism**

<table>
<thead>
<tr>
<th>Paradigm</th>
<th>Positivism</th>
<th>Interpretivism / Constructionism</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ontology</strong></td>
<td><strong>Realism:</strong></td>
<td><strong>Relativism:</strong></td>
</tr>
<tr>
<td>Belief about nature of reality</td>
<td>Truth is static and measurable</td>
<td>Meaning, rather than truth</td>
</tr>
<tr>
<td><strong>Epistemology</strong></td>
<td><strong>Objective:</strong></td>
<td><strong>Interactive:</strong></td>
</tr>
<tr>
<td>Belief about nature of knowledge &amp; acquiring it</td>
<td>Dualist</td>
<td>Transactional</td>
</tr>
<tr>
<td><strong>Methodology</strong></td>
<td><strong>Quantitative:</strong></td>
<td><strong>Qualitative:</strong></td>
</tr>
<tr>
<td>General approach to studying research topics</td>
<td>Experimental</td>
<td>Interpretative</td>
</tr>
<tr>
<td></td>
<td>Hypothesis testing</td>
<td>Exploratory</td>
</tr>
<tr>
<td></td>
<td>Deductive</td>
<td>Inductive</td>
</tr>
<tr>
<td></td>
<td>Context free</td>
<td>Context defined</td>
</tr>
</tbody>
</table>

Positivists search for the one constant truth, looking for facts about reality (ontology). This results in the researcher ideally maintaining a distance from the researched, in order to prevent the researcher influencing the results (epistemology). The methodologies aligned to this paradigm are therefore
experimental, or hypothesis testing. Traditionally, within this paradigm quantitative measures were considered superior [98].

The contrasting paradigm is interpretivism or constructivism. Interpretivists believe that truths are subjective, dynamic and contextual (ontology), and that we do not find or measure knowledge, but that it is constructed based on interactions with the social environment, so researcher and participants are considered co-creators of the findings, as the data itself is generated by this interaction (epistemology). This therefore influences the methodologies usually used which are described as qualitative, explorative, or interpretative and attempt to include an understanding of the context in which data are generated [98].

It is true that although certain principles or perspectives align to one or the other overarching paradigm, they are not fixed. For example, it is not unusual for a research question with a positivist orientation to be answered, at least in part, by qualitative methods. Despite this, I find the figure above (Figure 3.1) a useful, if slightly simplistic, summary.

To me, the fundamental difference between these opposing paradigms is that interpretivists reject the notion that an objective reality, or one true, reality exists, and believe that it is possible to have multiple realities that can be conflicting but all considered to be true at the same time. For example, participants may interpret the same events in different ways, which may be flatly contradictory, but their experience of the event remains true. This idea of whether the one true answer to the question is out there just waiting to be measured, or whether I needed to generate the knowledge through interacting with participants was fundamental in informing my choice of methods, and understanding them.

### 3.4 Generating research questions

I am first going to describe how I generated my research questions. In the subsequent section I will then discuss the methodological considerations associated with each of them.
As described in chapter 1, the project involved developing a complex intervention in the form of a website aiming to support self-management in adults with asthma. The obvious place for guidance on methodology was the Medical Research Councils (MRC) publication ‘Developing & Evaluating complex interventions: new guidance’ [100]. This guidance:

“is primarily intended to help researchers choose and implement appropriate methods, given the state of existing knowledge and the nature of their target intervention” pg 6

I found the following paragraph in the MRC guidance particularly illustrative of the problems faced by researchers in this field, and it became integral to my plans for how this project should progress:

“Developing, piloting, evaluating, reporting and implementing a complex intervention can be a lengthy process. All of the stages are important, and too strong a focus on the main evaluation, to the neglect of adequate development and piloting work, or proper consideration of the practical issues of implementation, will result in weaker interventions, that are harder to evaluate, less likely to be implemented and less likely to be worth implementing.” pg 4.

This process is illustrated in Figure 3.2 which shows the key stages recommended when developing a complex intervention [100], highlighting those covered in this project with **.

**Figure 3.2 Key elements of the development & evaluation process.**

I was determined that this project would follow best practice, and this framework strongly influenced what knowledge I felt was important to gain during the process, which in turn guided my research questions. Considering the development phase first, this guidance recommends three main stages: 1) identifying the evidence, 2) identifying or developing theory, and 3) modelling process and outcomes. This was followed by a fourth stage: feasibility and piloting. I will describe how consideration to these four stages in turn influenced my research questions.

3.4.1 Stage 1: Development - identifying the evidence base

The first of these recommendations appeared most straightforward, with the framework itself recommending a systematic review if possible, the only time it really specifies a specific methodological approach. When I considered what information I wanted from the literature this led to the generation of research question 1:

RQ 1: What is known about the effects of online tools to promote self-management of asthma and what helps or hinders their utilisation by patients?

3.4.2 Stage 2: Development – identifying or developing theory

The MRC guidance states;

“a vitally important early task is to develop a theoretical understanding of the likely process of change, by drawing on existing evidence and theory, and supplemented if necessary by new primary research, for example interviews with ‘stakeholders’, i.e. those targeted by the intervention, or involved in its development or delivery.”

I anticipated that my systematic review would contribute towards understanding the existing evidence, but what was less clear to me was what ‘a theoretical understanding of the likely process of change’ entailed for this project. On page 4, the guidance asks:
“Does your intervention have a coherent theoretical basis? Have you used this theory systematically to develop the intervention?”

As a novice researcher, with little formal training in social science or psychology, interpreting this recommendation was difficult for me. Even understanding definitions of what ‘theory’ meant was problematic as the language used was too alien to me. I found this definition useful initially [101]:

“a theory is a coherent conceptual arrangement that, when it is operationalized, makes possible a rational description and taxonomy of phenomena and constructs by which their systematic explanation is possible. From these stem a set of knowledge claims that, in turn, offer the potential for hypotheses or propositions that might be open to further investigation.” Page 539.

However, it suggests, as does the MRC Guidance, that researchers should choose a single ‘theory’ for a given intervention and I struggled to understand how that would work in practice for this project. I felt the literature about using theory was inaccessible to me, and I was subsequently relieved to discover I was not alone, and this is recognised reaction. As Davidoff et al [102] state in their useful overview:

“We also acknowledge that the term ‘theory’ itself can make people’s eyes glaze over, because ‘theory’ is seen as something abstract, intimidating and irrelevant, especially when their immediate and true concern is the hard work at the sharp end of providing care, rather than theory itself.” Pg 2

I certainly felt intimidated by it, and it was only by using it in practice during this fellowship, and through many discussions with supervisors and the expert panel that I have come to an understanding of what ‘theory informed’ really meant for this project.

There were two areas where theoretical underpinning was considered essential: deciding on the content of the website (understanding the likely processes of change), and when planning implementation processes. Therefore both behaviour change theory and implementation theory was used. I describe each of these in turn below.
3.4.2.1 Understanding the likely processes of change using behaviour change theory

In terms of ‘understanding the likely processes of change’, behaviour change theory was investigated. Behavioural theories such as Theory of Planned Behaviour [103] or Social Cognition Theory [104] have been shown to be useful in trying to understand and predict the steps involved in developing an intention to change behaviour, and then being able to act, including in asthma related interventions [105]. However, there is no evidence that asthma interventions based on these theories are any more successful than those which do not have a theoretical basis, and no evidence that any single theory is better in improving outcomes in asthma.

A lack of consensus when describing behaviour change interventions has increasingly been recognised in the literature [106]. In response to these issues a research programme was initiated to try and describe the individual constructs within established theories which predict behaviour change (rather than simply predicting behaviour) [106]. This has led to the publication of a taxonomy of behaviour change techniques (BCTs) which are derived from these established behaviour change theories, along with empirical evidence, and uses accessible language [107]. The intention of this taxonomy is that if all interventions include a description of which BCTs they include, then subsequent meta-analyses will be able to identify which are likely to be most effective to change which behaviours.

The absence of evidence that any individual behaviour change theory is superior when developing digital asthma interventions, and the presence of the taxonomy of behaviour change techniques, led to the decision to include as many BCTs as seemed relevant and to carefully map which BCTs were used, rather than choosing one specific behaviour change theory. How I decided on which behaviours to try to modify, with which BCTs, is described in later sections in this chapter.
3.4.2.2 Implementation theory – Normalisation Process Theory

The MRC Framework is clear: it is important to give early consideration to understanding implementation [100]. Normalisation Process Theory (NPT) is a mid-range implementation theory that is “concerned with the social organisation of the work (implementation) of making practices routine elements of everyday life (embedding) and of sustaining embedded practices in their social contexts (integration)” [101] pg 538

It was developed in response to the evidence that this implementation, embedding and integration rarely happens in practice [101, 108]. Although relatively new, NPT is increasingly being established as a useful implementation theory to understand the implementation of complex interventions [101, 109]. Its use to frame analysis in a meta-review of factors which promote or inhibit implementation of e-health systems illustrated that much of the published literature focused on organisational issues, neglecting the potential effects of roles and responsibilities, engagement of health professionals, and the importance of ongoing evaluation and feedback for improving implementation [110].

NPT suggests that for changes in behaviour (in this case improved asthma self-management such as taking inhaled steroids regularly) to become routine, people need to: understand what the new behaviours are and make sense of them (coherence); buy into these new behaviours and be willing to commit to them (cognitive participation); are able to operationalise the new behaviours and for changes in their workload to be acceptable to them and those around them (collective action); and finally in order for new behaviours to become truly embedded over time people need to judge the utility and effectiveness of these new behaviours and place value on them for themselves and those around them (reflexive monitoring). When we are considering a complex intervention to change behaviour these constructs can also be applied to the work of undertaking the desired behaviours, but also the work of engaging in the intervention which is promoting the desired behaviours. Murray et al [111] have argued that applying this framework when developing a complex intervention, alongside behaviour change theory, can help with its eventual successful
implementation. Therefore I used NPT from the earliest development stages such as informing focus group and think aloud study topic guides, and subsequently undertaking an ‘NPT analysis’ on the intervention during development as recommended by Murray et al [111].

A final role for NPT in a project such as this is to try and understand how feasible the evaluation is likely to be [111]. In this role it can be seen as a ‘trial killer’, where the result of the NPT analysis may actually suggest that either the intervention itself is not likely to be implementable and progression to an evaluation is not appropriate, or the evaluation itself is not going to yield the required information and itself needs reviewed. I undertook an ‘NPT analysis‘ of the trial parameters as outlined by Murray et al [111], and this is described fully in chapter 6.

NPT was also used as a framework to conceptualise qualitative data collected as part of a parallel process evaluation undertaken by a colleague.

In summary, NPT is increasingly being used for both informing the development of interventions in relations to how easy they are to implement and use, and understanding the likely success of their evaluation. I found it useful for both these functions.

### 3.4.2.3 Role of primary research

While I planned to use the metareview to gain an understanding of the existing literature, as per the MRC Guidance I also realised that primary research was essential here. I wanted to really understand why people here did not manage their asthma optimally, and what those who were currently experiencing asthma believed could help them to do it more effectively. I was particularly interested in exploring any differing perspectives between those whose behaviour we wanted to change (adults with asthma), and those who were currently best placed to support this (practice nurses). Including practice nurses in the primary research would have a further additional benefit: while I anticipated that this intervention should be a standalone resource, for patients to engage with it
‘approval’ from health professionals would be desirable, in particular practice nurses. This aspect of planning work has been shown to be often neglected in published eHealth interventions [110]. Belief in the usefulness of a resource is one of the strongest attitudinal predictors of intended future use [30] so having practice nurses promoting it could be an important determinant of its future uptake. This information would feed into our ‘model’ of how we anticipated our intervention would lead to behaviour change.

From this, I generated my second research questions:

RQ 2: What are the barriers and facilitators to the uptake and utilisation of a web-based self-management tool from the perspective of adults with asthma, and primary care nurses who undertake asthma reviews?

Therefore it can be seen that even at this early stage in the project I planned to use different sources to help me develop this intervention, such as theories (e.g. NPT), frameworks (MRC Guidance, BCT taxonomy) and also findings from new primary research (focus groups initially). These sources along with the experience of the expert panel would contribute to our understanding of how our intervention should work, allowing us to develop a model of the behaviours we want to change, and the expected impact on outcomes, similar to the process described in Davidoff et al of developing what they call a programme theory [102]. They define a programme theory as:

“a ‘small theory’ for each intervention……such theories are purposefully practical and accessibly; they are specific to each programme or intervention” pg 3

While this paper was not published at the time of the development of this intervention, it validates the approach we took of using existing evidence, theories and our own experiences (via the expert panel) to contribute towards our understanding of how the intervention would work [102]:

“Formal theory complements informal, experience-based theory, helping to define areas of dysfunction in health care systems, pinpoint their loci and identify their possible mechanisms.” Pg 9

So it is clear that this project drew on various sources. This makes sense for a project such as this, as it is increasingly being recognised that to change
outcomes, interventions need to work on multiple levels, and a ‘one theory fits all’ approach is increasingly seen as inadequate [112]. How these various sources of information were used in practice will be covered in more detail in relation to their associated research question below, or in their relevant chapter.

3.4.3 Stage 3: Development - modelling process and outcomes

Answering these first two research questions should provide the knowledge I needed to understand how this intervention should work, what should its ‘active ingredients’ be, and to work towards developing what has been referred to as a ‘programme theory’ [102] to explain essentially what I expected the intervention to do. The logical next step was then to consider actually making the intervention, in this case a website. This website should include these ‘active ingredients’ and promote changes in the specific behaviours we were targeting. Importantly I did not want to just develop an intervention based on this static collection of knowledge. Intuitively it felt right that while an initial draft could be developed based on RQ 1 and 2, further input with potential end users was essential to further develop and refine the intervention, testing out whether my interpretation of the literature, theory and stakeholders views resonated with potential end users. The MRC Framework states:

“before undertaking a substantial evaluation you should first develop the intervention to the point where it can reasonably be expected to have a worthwhile effect” pg 9

Additional user testing at this stage would therefore be warranted to ensure that the prototype developed from the findings from RQ 1 and 2 was optimised as much as possible prior to any pilot evaluation. Similarly, NPT could be used here in its ‘trial killer’ role: assessing there were any intervention related factors which could be barriers to implementation, allowing any alterations to be made at this early development stage [111].

With consideration to modelling outcomes, the MRC guidance specifically mentions the RE-AIM framework (Reach, Efficacy, Adoption, Implementation and Maintenance) [113]. This framework is promoted as a way of guiding evaluation methods, ensuring that researchers think beyond whether the intervention will work in the trial setting or not, to consider the broader picture of how it will
perform in real life settings. Therefore we aimed to use this framework to inform the choice of outcomes we would use our evaluation, as is explained in further detail in Chapter 6 (RCT).

While I was following best practice by drawing on multiple sources to inform the planning of the intervention, I genuinely did not know if or how these divergent sources of knowledge and experience could be pulled together to successfully inform the makeup of a behaviour change website. This led to the generation of my third research question:

**RQ3:** Can evidence from the literature (asthma management and theory) and input from potential end users, be successfully incorporated into an intervention to promote self-management?

Ideally, by this stage in the project I would have an intervention ready for preliminary testing in a pilot randomised controlled trial (RCT).

### 3.4.4 Stage 4: Feasibility and piloting

In alignment with the MRC framework (Figure 3.2) the next phase would then be to embark on the feasibility and piloting stage. The rationale behind including such a phase is clear: it aims to reduce the number of studies that are undermined by issues which would have been anticipated by appropriate piloting, such as poor recruitment, high attrition, and smaller than expected effect sizes [100]. With an intervention such as this there would be outcomes common to any complex intervention which would be important to measure such as recruitment and retention and how much was the intervention actually used by participants. Secondly, as informed by our use of the RE-AIM framework [113] I was also interested in how this intervention might improve outcomes for those it targeted, particularly in terms of symptoms and quality of life. This led to generation of the fourth and final research question:

**RQ4:** What would be the feasibility of undertaking a randomised controlled trial of Living Well with Asthma, and how would such a website be used by adults with asthma. What would be the effect on symptom scores and quality of life measures?

As part of this evaluation it would be ideal to undertaken qualitative interviews with intervention group participants to explore experiences of using the
Chapter 3 Methodological Considerations

intervention, and also of participating in the evaluation itself [100]. Doing this myself however was impossible within my timescales, but fortunately a colleague was able to undertake this work separately.

3.5 Choosing methods appropriate to the research questions

In this section, I am going to look at each research question (RQ) in turn in more detail, and consider how the research questions themselves guided me when choosing my research methods.

3.5.1 Research question 1

RQ 1 - What is known about the effects of online tools to promote self-management of asthma, and what helps or hinders their utilisation by patients?

My initial research question appeared to be answered best by undertaking a systematic review, a method recommended within the MRC framework I was using. Historically this would have automatically referred to a review of quantitative papers, possibly resulting in either a meta-analysis or narrative synthesis. However, I had three issues to consider when choosing the specific method for this stage. The first was that the literature on asthma self-management was vast. The second was that I was keen to try to establish what helped or hindered the use of digital self-management interventions that was unlikely to be answered by quantitative methods alone. The final issue was that I was comparatively time limited, as I wanted to ensure I allowed adequate time for the subsequent website development and evaluation phases of the project.

Epistemologically the second issue did not sit well within a positivist paradigm, as I did not want to simply quantify who was hindered, but I wanted to understand the why, and to generate new data about what would help or hinder use of digital interventions, a stance which lends itself more to research methods within an interpretivist paradigm. However, to truly work in this paradigm requires a relationship between the researcher and the researched, a
tenet that would be impossible if systematic review was to be the underlying methodology. This was a debate I had been involved in during work preceding my fellowship when I participated in a synthesis of qualitative papers exploring treatment burden in stroke [45, 46]. Although there were concerns raised about the ability of this method to generate rich new knowledge, in practice for this previous project such an approach had worked very well. The results of the stroke review provided new and illustrative findings which could not have been generated by looking at the articles in isolation. It was thought these methods were transferrable to this current project, and would contribute to answering this research question.

Therefore I decided that undertaking a systematic review of both quantitative and qualitative articles was essential to try and build a rich picture of how effective these interventions were in practice, and what helped and hindered their use. In response to concerns about timescales and the vastness of the literature we concluded a meta-review (systematic review of systematic reviews) would be a useful method in view of my tight timescale and given this method had recently been found to be helpful previously [110]. I anticipated it would reduce the number of articles being synthesised to a manageable number, yet still providing a comprehensive overview of what was known on the subject.

In addition to this systematic review, as part of the University of Glasgow postgraduate research requirements I also completed a more generalised literature review on the topic of asthma and self-management which also informed the intervention. This was updated and formed the basis of Chapter 2.

3.5.2 Research question 2

RQ 2 - What are the barriers and facilitators to the uptake and utilisation of a web-based self-management tool from the perspective of adults with asthma, and primary care nurses who undertake asthma reviews?

Epistemologically this was far more straightforward. Barbour [114] discusses the differences between data generation and data collection, and this was firmly in the former. Here I wanted to understand how individuals managed their asthma, and explore their own personal barriers and facilitators to doing so.
Understanding the context was crucial particularly to allow me to be sensitive to change [114], a particular issue in the fast moving field of eHealth. Here I also wanted to produce ideas about what the intervention I was going to make should or could contain, in order to be clear about its likely ‘active ingredients’. The interaction between myself and the participants would be critical to the data generated and we would be co-creators of the findings. However true interpretivism implies that this process is entirely explorative and pre-defined theories are actively discouraged. This was a stance I could not justify, as I wanted to build on the data from the literature, and my own clinical experience could not be ignored. Ultimately I decided that I would use key findings from the preceding literature review as discussion prompts, thereafter focusing on the generation of new data. As discussed in the preceding section I anticipated the dialogue between adults with asthma and practice nurses undertaking asthma reviews (and therefore promoting self-management) would be the most valuable source of knowledge to answer this research question. Therefore, heterogeneous focus groups were planned, with both practice nurses and people with asthma as participants. Here I wanted to focus in on the barriers and facilitators to the participants undertaking self-management practices with a view of really understanding what might a digital intervention do to facilitate it, and how it would potentially be operationalised in practice. To this end I elected to use normalisation process theory (NPT) [101, 108] to inform the focus group topic guide, and planned to use it as a framework to inform the analysis of the anonymised transcripts from the focus groups.

Using this framework would ensure I would be in a position to explore any suggested features both in terms of how they could be incorporated into the intervention for this evaluation, but also how might that work both in a trial setting, and importantly in everyday life should the intervention be ultimately proven to be acceptable and effective [111].

### 3.5.3 Research question 3

**RQ 3** - Can evidence from the literature (on asthma management and theory) and input from potential end users, be successfully incorporated into an intervention to promote self-management?
To answer this research question would require two different stages. Firstly, it involved me gaining an understanding of how this intervention would work in practice - developing our own model for the intervention to explain our proposed mechanisms of action. Secondly, it refers to the practical process of turning our understanding of the likely mechanisms of action into a working, interactive behaviour change resource. From a practical point of view how I undertake the process for the first stage above, developing our intervention model, eluded me until I read Campbell et al’s article on designing and evaluating complex interventions to improve health care [115]. The authors summarise this as follows:

“The essential process involves mapping out the mechanisms and pathways proposed to lead from the intervention to the desired outcomes, then adding evidence and data to this map.”

This article emphasised the importance of defining and understanding the problem through 5 key tasks. Having an understanding of the literature was essential to complete these tasks, and this process is described in full in chapter 5.

During the development process as I developed a prototype of the website I regularly undertook a 'NPT analysis' of the developing website, using this theory in its potential ‘trial killer’ role [111], to ensure that even at these early stages we were developing something that should be implementable in the long term.

Regarding the second phase: there is some guidance on strategies that involve end users during development phases, with think aloud studies being the single most recommended strategy [32, 116, 117]. Importantly two advisors to the project Prof Lucy Yardley and Dr McGee-Lennon had experience of using this technique and were able to provide direct guidance on the methods. Epistemologically this phase was aiming to corroborate our findings from earlier stages as users went through sample pages of the website providing their own personal viewpoint of its contents; however, I was also keen to encourage the participants to volunteer their own solutions to any issues or concerns they had with the content, or any gaps in its scope. Again, the participants were co-creating the findings with me as we worked through the prototype pages. NPT was used here to inform the topic guide, and in particular the questions I asked
at the end of the think aloud study about how they would use the intervention in real life.

I chose to use an open source software called LifeGuide [118, 119] to develop this intervention. Lifeguide was designed for researchers like me without a background in computer programming. Using this software allowed me to directly develop and modify web pages without reliance on specialised programming support, which is costly and time consuming. Capability for modifying a resource such as this during development is recommended by the MRC Framework [100], and a meta-review of factors which promote or inhibit implementation of e-health systems highlighted the importance of on-going evaluation and feedback for improving implementation potential [110].

3.5.4 Research question 4

RQ 4 - What would be the feasibility of undertaking a randomised controlled trial of Living Well with Asthma, and how would such a website be used by adults with asthma. What are the effect on symptom scores and quality of life measures?

Randomisation is considered the ‘gold standard’ when evaluating a new intervention, however there was a choice to make when deciding whether this should feature in this project? Should this be a single arm, feasibility study, where all enrolled get the intervention and the results work towards improving and refining both the intervention and trial processes? Or should we aim to have a pilot study - the main trial run in miniature so to speak, in order to estimate recruitment retention and effect sizes. As is clear from chapter 1 we decided to do both, a pilot study with feasibility outcomes, believing that we could achieve both.

Given this research question centred on a RCT, quantitative measures were clearly going to take precedence. As described earlier the RE-AIM Framework [113] was used to inform our evaluation methods, and it’s use is described fully in the methods section of Chapter 6. This was particularly helpful in encouraging me to think beyond the obvious quantitative outcomes such as symptom scores to include relevant process outcomes such as web usage that
would contribute towards decisions about whether the intervention should be taken forward to full RCT in the future.

In addition to RE-AIM framework to guide choice of outcome measures I also undertook a NPT analysis of the trial procedures to ensure the trial itself was feasible, and compatible with the environment we were undertaking it in. Again full details are found in Chapter 6.

3.6 Conclusion

I have included this separate methodology chapter in order to fully describe the rationale behind my choice of research questions and subsequent methods, providing a more in depth understanding of the thought processes that went into some of the major decisions made within this project. This illustrates the excellent learning experience afforded to me by undertaking this project, particularly given that I was primarily involved in these decisions, rather than undertaking project where the methods had been already confirmed.
Chapter 4: Meta-review of Digital Asthma Self-Management Interventions

4.1 Introduction and aims

This chapter details the methods, results and findings from a meta-review of quantitative, qualitative and narrative systematic reviews as well as meta-syntheses or meta-ethnographies of articles describing digital self-management interventions. A meta-review is a term used to describe a systematic review of systematic reviews. Other terms used in the literature include overview, or umbrella review, however these terms can also be used to describe non-systematic reviews (e.g. opinion pieces), therefore the term meta-review is used here for this chapter. The aim of this meta-review was to establish what was already known in the literature about the effects of digital online tools for self-management of asthma, and if possible, to establish what helps or hinders their utilisation by patients.

4.1.1 Contributors

I planned this review with the support of my PhD supervisory team. I led all stages; however as is considered best practice, many of these stages required the assistance of a second person, such as for screening articles and quality appraisal. This role was undertaken by a range of people and they are referred to in the methods sections by their initials. Table 4.1 below lists those who contributed in alphabetical order.

<table>
<thead>
<tr>
<th>Initials used</th>
<th>Full name</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMC</td>
<td>Alex McConnachie</td>
</tr>
<tr>
<td>AMM</td>
<td>Alison M MacKenzie</td>
</tr>
<tr>
<td>DM</td>
<td>Deborah Morrison</td>
</tr>
<tr>
<td>EC</td>
<td>Euan J Cameron</td>
</tr>
<tr>
<td>FM</td>
<td>Frances S Mair</td>
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<tr>
<td>KA</td>
<td>Karolina Agur</td>
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<tr>
<td>NCT</td>
<td>Neil C Thomson</td>
</tr>
<tr>
<td>RD</td>
<td>Robert I Docking</td>
</tr>
<tr>
<td>SW</td>
<td>Sally Wyke</td>
</tr>
<tr>
<td>VD</td>
<td>Vandana Raghuvir</td>
</tr>
</tbody>
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4.2 Methods

4.2.1 Rationale

As described fully in Chapter 3, meta-review was chosen as a methodology to allow me to quickly gain a snapshot of the literature to inform the subsequent phases of the PhD, in particular intervention development. Undertaking systematic review of the literature prior to developing an intervention fits with the MRC Complex intervention development framework.

4.2.2 Protocol development

A copy of the final protocol for this meta-review can be found in appendix 4. Much discussion was needed to clarify inclusion and exclusion criteria, streamline data extraction and finalise the review protocol. The process involved the development of multiple iterations of the protocol which were refined in discussions between the supervisory team and I, and then the final protocol was approved by all PhD supervisors. As is considered good practice the intention was to register the protocol on PROSPERO which is an international prospective register of systematic reviews (http://www.crd.york.ac.uk/PROSPERO/). Unfortunately, at the time the review was undertaken, they did not accept systematic reviews of systematic reviews. Following advice from my external examiners I updated the protocol in January 2016 to remove the AMSTAR score as a criterion for inclusion. This was to allow me to include all identified reviews, regardless of quality, and therefore provide a comment on their methodological quality. This was considered preferable as it would increase the number of reviews available to include in this metareview providing a broader picture of the literature to date.

4.2.3 Inclusion & exclusion criteria

We defined our inclusion and exclusion criteria using the PICOS framework (participants, interventions, comparators, outcomes, study design) as recommended by the Cochrane collaboration [120]. Table 4.2 describes the inclusion criteria.
Table 4.2 Inclusion Criteria

<table>
<thead>
<tr>
<th>Participants</th>
<th>Those with asthma of any age, or their carers.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Online or computerised interventions facilitating self-management through education and/or providing advice or other behavior change approach. We only included interventions which provided these features independent of any health professional input. Interventions delivered by computer, tablet, smartphone, or purpose built electronic device were included.</td>
</tr>
<tr>
<td>Comparison</td>
<td>Usual care, or other forms of self-management interventions such as face to face education, or written information.</td>
</tr>
</tbody>
</table>
| Outcomes     | We examined any available evidence relating to the following primary outcomes:  
- Activity limitation (e.g. days off work/school/disturbed nights)  
- Adverse events  
- Barriers and facilitators to online asthma intervention use by patients and practitioners  
- Biomarkers of airway inflammation (e.g. exhaled nitric oxide)  
- Health service utilization (including scheduled/unscheduled, and primary/secondary care)  
- Lung function (e.g. spirometry & reversibility, peak expiratory flow (PEF))  
- Medication use (e.g. relief inhaled β agonist use, compliance with medication)  
- Quality of life  
- Symptoms (measures of asthma control, e.g. diary card scores, asthma control questionnaire, exacerbation rates)  
We also examined any available evidence relating to the following secondary outcomes:  
- Markers of self-management (e.g. adherence to monitoring tools, use of action plans, self-efficacy)  
- Patient knowledge  
- Patient satisfaction  
- Recruitment, retention rates  
- Cost effectiveness  
- Use of behavior change theory during intervention development and implementation processes |

Study design: Systematic reviews describing interventions as outlined above (see below for full definition.

For clarity, it was helpful to specify certain exclusions when considering the interventions, outcomes and study design as shown in Table 4.3.

Table 4.3 Exclusion criteria

| Intervention | Reviews featuring interventions which comprised only of telemonitoring or clinical decision support software for health professionals were excluded. Interventions which only provided a means of self-monitoring without providing feedback directly were excluded. For example electronic diaries for recording peak flows or symptoms, which did not provide automated feedback, were excluded. The content of the intervention was required to be delivered at least in part by the digital medium itself. Devices which were simply digital modes of communicating between patients and health professionals were excluded. |
| Outcomes     | Reviews which did not provide information specific to our outcomes of interest were excluded. |
| Study Design | See below |
To define what we meant by a review we used the definition developed by Mair et al. [110] for use in their meta-review, outlined below.

“We considered a review paper to be one that provides an analytic account of the research literature related to a specific topic or closely related set of topics. It is intended to contribute to knowledge by answering a research question. Thus, we include the following types of papers:

1. Systematic reviews: where relevant literature has been identified by means of structured search of bibliographic and other databases; where transparent methodological criteria are used to exclude papers that do not meet an explicit methodological benchmark, and which presents rigorous conclusions about outcomes.
2. Narrative reviews: where relevant literature has been purposively sampled from a field of research; where theoretical or topical criteria are used to include papers on the grounds of type, relevance, and perceived significance; with the aim of summarising, discussing, and critiquing conclusions.
3. Qualitative meta-syntheses or meta-ethnographies: where relevant literature has been identified by means of a structured search of bibliographic and other databases, where transparent methods had been used to draw together theoretical products, with the aim of elaborating and extending theory.
We excluded the following:

1. Secondary analyses (including qualitative meta-syntheses or meta-ethnographies) of existing data-sets for the purposes of presenting cumulative outcomes from personal research programs.
2. Secondary analyses (including qualitative meta-syntheses or meta-ethnographies) of existing data-sets for the purposes of presenting integrative outcomes from different research programs.
3. Discussions of literature included in contributions to theory building or critique.
4. Summaries of literature for the purposes of information or commentary.
5. Editorial discussions that argue the case for a field of research or a course of action.

Where the abstract states it is a review, but there is no supporting evidence in the main paper, such as details of databases searched or criteria for selection of papers (either on methodological or theoretical grounds), the paper is excluded."

4.2.4 Information sources & search strategy

4.2.4.1 Electronic Search Strategy

A professional systematic review company (York Health Economic Consortium, YHEC), searched a wide range of databases covering health, mental health, education, and social science (14 in total), with no start date until July 2011. The search strategy was devised using a combination of subject indexing terms (e.g. MeSH in MEDLINE), and free text search terms in the title and abstract. The search terms were identified through discussion between the supervisory team, and by scanning background literature, and browsing database thesauri. To ensure sensitivity the search strategy did not include a methodological search filter to limit to reviews. The searches were not limited by date range or language.

The search strategy covered 3 broad areas:

1. Asthma and related terms
2. Online/computerised and related terms
3. Self-care/self-management, patient experience, qualitative and related terms
Searching was undertaken in two phases. The first was completed in July 2011. The second phase was in October 2013, due to a period of maternity leave. This brought the electronic search up to date, with the specific addition of terms relating to mhealth, which had become more prominent in the interim.

The full list of databases searched and an example of the full search strategy for MEDLINE is available in appendix 5.

4.2.4.2 Supplementary search strategies

We had agreed to use the term ‘respiratory’ alongside asthma and related terms, rather than ‘chronic disease’ in our electronic search strategy as a way of keeping the number of articles found at a manageable level. This meant there was the potential that a review including multiple disease areas may only index itself with terms such as chronic disease, which would not have been picked up by our search strategy. As a way of trying to capture such reviews the journal Patient Education and Counseling was hand searched as it was not limited to respiratory articles. In addition, the Primary Care Respiratory Journal was also hand searched. This was chosen as it was considered to be a typical journal that might feature reviews such as we were targeting. Experts in the field were also contacted to establish if any reviews had been missed.

To further increase the chances of picking up articles not found by the initial electronic search strategy the reference lists of included reviews were also hand searched, and the citations of included reviews also examined. Supplementary searching was not used in the second round of electronic searches in 2013, recognising the concerns that Cochrane Handbook discuss (section 10.2.2.3, citation bias) that “retrieving literature by scanning reference lists may thus produce a biased sample of studies” [121].

4.2.5 Study selection

4.2.5.1 Software

Distiller SR software was used for the article selection and data extraction (https://systematic-review.ca). This is a web based platform which allows multiple users to screen simultaneously. It can also be used to allocate articles
to specific users. Therefore, study selection processes could be set up so that I always had to be one of the reviewers for each individual article, and the second review could be done by any of the other contributors.

4.2.5.2 Article screening

Screening was undertaken by myself, plus one other independent researcher (EC, SW, FM, NCT, KA, RD, AM or VR), with close reference to the protocol. This was done at three individual levels - title, then abstract, then full paper. The process is illustrated in Table 4.4 below.

<table>
<thead>
<tr>
<th>Screening level</th>
<th>How many reviewers need to 'include' to proceed to next level</th>
<th>Process for managing conflicted reviews</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title</td>
<td>1</td>
<td>Automatically put through to abstract screening</td>
</tr>
<tr>
<td>Abstract</td>
<td>2</td>
<td>Discussed between initial reviewers, if conflict remains put through to full paper screening.</td>
</tr>
<tr>
<td>Full paper</td>
<td>2</td>
<td>Discussed between initial reviewers and if conflict remained, discussed with third party.</td>
</tr>
</tbody>
</table>

4.2.5.3 Quality appraisal

Given this was a review of reviews, and was an additional step away from the original data it was felt to be important to be able to comment on the quality of the included reviews, especially given the evidence that poor quality research may appear to inflate effect sizes [122, 123]. Lack of quality assessment of included reviews was a significant area of concern in a review paper describing this comparatively new method [124].

Quality appraisal was undertaken in two ways. First, at the full paper screening stage, papers were required to meet criteria laid out in our definition of a review. For example, evidence of a systematic search or criteria for selection of papers must be included (see section 4.2.3 earlier for the full definition).

Following this, all papers that were included at the full paper screening level then underwent formal quality appraisal using A Measurement Tool to Assess Systematic Reviews (AMSTAR) [125-127]. This 11 point checklist covers 7 key domains as listed in Table 4.5 below, and is available in full in appendix 6.
Scoring systematic reviews using guides such as AMSTAR has been recommended in the literature \[128\]. An AMSTAR score was assessed for each included review by me, and independently by a second reviewer (KA). Conflicts were to be discussed between reviewers initially and then with a third party (FM) if agreement could not be reached. AMSTAR score was used to assist in appraising the quality of the included reviews, and to inform the discussion. Articles were not excluded on the basis of their AMSTAR score.

### Table 4.5 AMSTAR domains

- Establishing the research question and inclusion criteria before the conduct of the review
- Data extraction by at least two independent data extractors
- Comprehensive literature review with searching of at least two databases
- Detailed list of included/excluded studies
- Quality assessment of included studies and consideration of quality assessments in analysis and conclusions
- Appropriate assessment of homogeneity
- Assessment of publication bias and a statement of any conflict of interest

### 4.2.6 Data collection

For each included review we collected:

1. General information about the review (year, aim, number of studies, search strategy information, outcomes, strengths and limitations).
2. Results for each outcome of interest (including quotes from qualitative/narrative reviews).

### 4.2.7 Data synthesis

Any quantitative data relating to outcomes of interest were extracted and reported either as a meta-analyses if the data allowed or more likely as a narrative summary if the data were too heterogeneous. Where qualitative data was extracted meta-synthesis would be undertaken.
4.3 Results

4.3.1 Article searching & screening

4.3.1.1 Search results

Results refer to articles found from both searches combined.

Electronic and supplementary searching found 6983 articles: following removal of duplicates this left 3810 individual articles to screen.

The full report from YHEC detailing search terms and results per databases can be found in appendix 5.

The flow of articles is illustrated in Figure 4.1

Figure 4.1 Flow of articles

4.3.1.2 Reasons for exclusion

There were three main reasons for articles being excluded. Firstly on examination of the full paper it was clear that many included studies featured participants with diseases other than asthma. Secondly, on close examination it was evident that reviews included studies involving interventions that did not
meet our criteria of being an interactive digital intervention that could function at least in part without input from health professionals. It had not been anticipated that such a large number of reviews would fail to meet this inclusion criteria. The main reason for this was the dominance of studies involving tele-monitoring interventions, which did not provide feedback without input from a health professional. The final and most common reason for exclusion was that the article did not meet our definition of a review. The majority of the reviews excluded for this reason were articles that called themselves a review, but on close reading did not fulfil our definition of a review, as described in the preceding section. The following extract from our aforementioned definition of a review led to many articles being excluded:

“Where the abstract states it is a review, but there is no supporting evidence in the main paper, such as details of databases searched or criteria for selection of papers (either on methodological or theoretical grounds), the paper is excluded.”

This was particularly true of those papers using qualitative methodology, and was the main reason why this review had fewer articles than anticipated.

4.3.2 Description of included review

This section describes the 1 review which met our full paper screening criteria, summarised in Table 4.6 below [129]. The article contained 9 RCTs, only two of which were aimed at adults. Bussey-Smith summarised follow up as ranging from 4 to 12 months, but then commented on several studies with a 12 week follow up which is confusing for the reader. Dropout rates were summarised by Bussey-Smith [129] as ranging from 0% to 31%.
4.3.2.1 Quality appraisal

The AMSTAR score of the one included review [129] was 27%, and the full details underpinning the AMSTAR score are shown in Table 4.7. The article received 3 points (comprehensive literature search, characteristics of included studies, and methods to combine appropriate). Table 4.7 shows that the main areas where points were lost were around absence of a review protocol, restriction of search terms by use of language and study type filters and the absence of any assessment of quality of their included articles. While they were clear there was duplicate data extraction, it was not clear whether this was the case for screening. AMSTAR requires publication bias be assessed or at least some comment about why it was not, and this was also missing from this review. Although the authors of the review provided information about their own conflicts of interest, they did not do so about their included studies and therefore they did not receive a point for question 11. Importantly the review makes no mention of the quality of the included studies, either in the description of the included studies or in the discussion.
Table 4.7 AMSTAR results of included review

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Was an “a priori” design provided?</td>
<td>No</td>
</tr>
<tr>
<td>2 Was there duplicate study selection and data extraction?</td>
<td>Can’t answer</td>
</tr>
<tr>
<td>3 Was a comprehensive literature search performed?</td>
<td>Yes</td>
</tr>
<tr>
<td>4 Did the authors state that they searched for reports regardless of their publication type? Was the status of publication (i.e. grey literature) used as an inclusion criterion?</td>
<td>No</td>
</tr>
<tr>
<td>5 Was a list of studies (included and excluded) provided?</td>
<td>No</td>
</tr>
<tr>
<td>6 Were the characteristics of the included studies provided?</td>
<td>Yes</td>
</tr>
<tr>
<td>7 Was the scientific quality of the included studies assessed and documented?</td>
<td>No</td>
</tr>
<tr>
<td>8 Was the scientific quality of the included studies used appropriately in formulating conclusions?</td>
<td>No</td>
</tr>
<tr>
<td>9 Were the methods used to combine the findings of studies appropriate?</td>
<td>Yes</td>
</tr>
<tr>
<td>10 Was the likelihood of publication bias assessed?</td>
<td>No</td>
</tr>
<tr>
<td>11 Was the conflict of interest included?</td>
<td>No</td>
</tr>
</tbody>
</table>

4.3.2.2 Descriptions of participants & interventions

The featured review [129] included two RCTs aimed at adults and 7 RCTs aimed at children. The 9 RCTs included evaluated a total of 957 patients (471 control, 486 intervention), aged between 3 and 75 year of age. Dropout rates ranges from 0% to 31.7%. Study lengths ranged from 4 to 12 months. Included interventions were heterogeneous, with some to be used daily and others only as a one off, and some included the use of games/vignettes or provided self-monitoring tools.

4.3.2.3 Results for outcomes

As there was only one study meeting inclusion criteria [129] I will provide a summary of their results which are available for my outcomes of interest: symptoms, health service use, lung function, medication use and patient knowledge.

Primary outcomes

Bussey-Smith et al found evidence of improvement in symptoms. Hospitalisation rates and acute care visits were reported, but there was no clear picture about effectiveness on either outcome with the majority of studies reporting no significant difference. This was also true of lung function and medication use where the majority of studies reported no difference.
There were no results available for the remaining primary outcomes of interest:

- Activity limitation (e.g. days off work/school/disturbed nights)
- Adverse events
- Barriers and facilitators to online asthma intervention use by patients and practitioners
- Biomarkers of airway inflammation (e.g. exhaled nitric oxide)
- Quality of life

**Secondary outcomes**

Knowledge was a frequently measured outcome, and the majority of studies showed an improvement. There was a suggestion that time spent interacting with the digital intervention may be correlated with the improvement in knowledge, but not with any improvements in clinical outcomes, and they could draw no further conclusion about the type of delivery or content that appeared to be most successful.

There were no results available for the remaining secondary outcomes of interest:

- Markers of self-management (e.g. adherence to monitoring tools, use of action plans, self-efficacy)
- Patient satisfaction
- Cost effectiveness
- Use of behavior change theory during intervention development and implementation processes

Importantly this study commented on the improvements seen in many control groups, suggesting that this may be diluting any potential benefit, particularly as many control groups were not receiving merely usual care but rather an enhanced form of alternative care.

Overall, this systematic review concludes that interactive digital devices appear to improve knowledge and perceived symptoms, but that there is less evidence for improvement of objective clinical outcomes such as lung function, health care contacts or medication use. Importantly, the authors emphasize that the
published literature to date does not provide us with adequate detail to allow conclusions to be drawn regarding what features may be more likely to result in improved outcomes. Although not specifically reported as an outcome there was no evidence of harms to participants from being intervention groups, compared to control groups.

4.4 Discussion

4.4.1 Summary of findings

The search for this meta-review identified 3810 individual articles to screen, which following application of pre-defined inclusion and exclusion criteria led to only one systematic review being included. This was disappointing. There were three main reasons for the high exclusion rate: 1) firstly many reviews were a mix of asthma/non asthma studies, 2) many reviews included interventions not meeting our definition of a digital interventions, and 3) a higher number than expected did not meet our definition of a review, mainly in relation to suboptimal methods, or recording of methods.

The one article included featured nine RCTs aimed at adults or children and concluded that interactive resources appeared to improve symptoms and knowledge, with less evidence of benefit for clinical outcomes such as lung function, health care contacts or medication use. One important finding from this review is to highlight the importance of an appropriate control group during such evaluations. In particular, they noted that many control groups were receiving care superior to that provided in routine asthma care, possibly diluting any benefit attributable to the intervention under evaluation. This study was unable to draw any firm conclusions about what type of delivery or content appeared to be most successful at improving outcomes, other than a possible correlation between time spent interacting with the resource and improved knowledge.

The lack of economic data was disappointing, although the results on health care resource use (hospitalizations and ED visits) suggests that evidence of cost-effectiveness may be lacking. However without data including routine health
care resource utilization, and formal economic analysis, no firm conclusions can
be drawn. So this is clearly an outstanding gap in the published literature.

The authors of the study did not provide any quality appraisal of their included
studies which is a weakness. My own quality appraisal of this review used the
AMSTAR score and the review scored 3 out of 11 points. Other limitations of the
included review relate to lack of clarity about attrition rates and length of
follow up, and the fact that they did not acknowledge any limitations
themselves in their discussion, which in turn limits the conclusions which can be
drawn from this meta-review.

4.4.2 Methodological issues with meta-reviews

Due to the growing number of meta-reviews being published there is increasing
interest in the methodology being employed [124, 128, 130].

Smith et al in their methodology paper published in 2011 aimed to provide a
guide to clinicians and researchers who wish to conduct systematic reviews of
systematic reviews, and share their experiences [128]. This useful article
discusses challenges that may be encountered at five different stages when
conducting this type of review: 1) sources, 2) study selection 3) quality
assessment, 4) presentation of results, 5) implications for practice and research.
I will discuss the strengths and weaknesses of this meta-review using these
headings, and reflect generally on methodological concerns at each stage
individually.

4.4.2.1 Sources

The methodological challenges of undertaking a systematic review of reviews are
similar to a systematic review of the primary literature. A team (YHEC) with
excellent experience of undertaking systematic reviews, using multiple
databases, and using a strategy designed iteratively with researchers to be as
inclusive as possible, without being unwieldy, undertook the search. Therefore
the comprehensive nature of the search strategy is one strength of this review.
Studies published in languages other than English (LOE) were included, which is
also considered a strength of this review, and is recommended by the Cochrane
Collaboration (section 6.4.9 [131]). However, even they acknowledge that there
is increasing debate about how essential including reviews in LOE actually is, and suggest that it may be more of an issue historically, describing the marked decline in publications in LOE since 2006. A more recent meta-analysis [132] has investigated this question specifically and concluded from their review that there was no evidence of systematic bias from the use of a language restriction. However, this review only focussed on meta-analysis and they did note that their findings may not be generalizable to all fields of medicine. In particular, they reported that studies published in Chinese are important in certain research areas such as molecular medicine, and that LOE may be more important when reviewing studies focussing on psychiatry, orthopaedics and rheumatology. In addition they also commented there is conflicting information regarding whether there is a link between publication language and methodological quality, with some studies finding those published in LOE to be lower quality. This resonates with the experience from this review where four full papers were translated into English for assessment, and three articles, two in German and one in Chinese, did not meet our definition of a review due to poor methodology (e.g. no evidence of systematic search etc.). The final LOE paper was in Portuguese and this included interventions targeting other disease areas in addition to asthma.

Given the considerable workload implications and cost of including papers in LOE, it does seem on balance that using a language restriction may be acceptable, depending on the area of research.

Despite the comprehensive nature of the search it is possible the search may have missed reviews of chronic illness interventions including asthma but not specifically indexed with asthma or respiratory terms. The decision to include only those papers linked to respiratory terms was essential to ensure the search was not unwieldy, and remained manageable and our supplementary searching attempted to counter any potential disadvantages from taking this approach.

4.4.2.2 Study selection

Smith et al advise not to underestimate the importance of the planning stage, and in particular formulating the scope of the review with particular care over inclusion and exclusion criteria, and experience from this meta-review reinforces this message [128]. The rationale for undertaking a meta-review is to
create a summary of reviews in a single paper, thereby providing an overview of the published research in a given area and enable key gaps in knowledge to be identified. The low number of included papers in this review somewhat limits the learning possible from this meta-review, and the inclusion/exclusion criteria used in this meta-review using the PICOS format, are discussed below, along with reflections on what could have been done differently to enhance learning from the literature.

**Participants**
We included studies where participants of any age had asthma. Asthma is a common condition, and although some articles were excluded due to combining asthma with non-asthma participants it can be argued that this was a reasonable choice for this review. This is because asthma has its own specific issues less relevant to other disease areas, such as the potential ambiguity around diagnosis, underestimation of symptoms and treatment options which includes inhalers rather than tablets.

**Interventions**
The inclusion/exclusion criteria regarding the intervention type were very specific, for example the active exclusion of tele-monitoring interventions. The Cochrane handbook provides a table outlining typical objectives for undertaking meta-reviews, and in summary, they suggest that the rationale is usually either: 1) combining evidence for different interventions for the same condition; 2) where different outcomes are addressed in different reviews or; 3) similar interventions in different disease areas (page 611) [131]. As An de Sutter highlights in her editorial on this topic ‘the key word is different’, and that simply combining reviews on the same intervention for the same condition, may provide an overview of the topic, but adds little over a well conducted primary review of the literature [133]. It might have been useful to have included tele-monitoring interventions and this would have allowed us to compare and contrast the evidence for different types of interventions. We could have gone a step further to include digital and non-digital interventions and this may have provided useful insights into the potential added benefits of digital delivery of contents. The Cochrane Public Health Group consider having a broad research question a specific feature of this type of methodology, and allows for
generalisability [134] and while our research question was indeed broad, our inclusion/exclusion criteria did not reflect this. In hindsight if we wanted information about such a specific type of intervention a primary review of such interventions might have been more appropriate. However, we were eager to get a very broad overview of the subject including both qualitative and quantitative reviews and this would not have been feasible with a primary review within the context of this PhD, which has so many other components, hence the rationale for undertaking a meta-review.

Comparison Group
For this review, we did not have restrictions on what if any intervention the comparison group had, and on reflection, this still seems the correct approach for this meta-review.

Outcomes
This is an area where the available guidance could be interpreted as being conflicting. Smith et al [128] recommends having one primary outcome and focusing on this, suggesting that it allows the researcher to manage the workload by limiting data extraction to only those results relevant to the topic of interest from all the reviews that report on various different outcomes. This may be true in certain areas where there is a more limited range of potential outcomes. The example used in Smith et al’s meta-review methodology paper cited throughout this chapter is for interventions to reduce pre-term labour, where the potential ways of measuring success are arguably fewer than for asthma [128]. The vast range of asthma outcomes used across clinical trials has long been recognised as a barrier to successful synthesis of asthma literature, and as a result a workshop was convened in 2012 in order to provide guidance to researchers to try and streamline the outcomes used, and they found 7 distinct clinical research domains applicable to asthma, with several outcomes in each domain [135]. Therefore choosing to focus on one asthma outcome would likely miss important relevant information. In contrast to Smith et al’s recommendation, Cochrane specifically suggest that one rationale for undertaking an overview is to synthesise reviews where different outcomes are used for similar interventions - and this was what we aimed to do here. We elected to include a range of outcomes in order to be as inclusive as possible and
that was right for this review, and narrowing down to a single primary outcome would not be appropriate for asthma.

**Study type**

When finalising the inclusion/exclusion criteria regarding study type, the definition of a systematic review was based on a previous meta-review undertaken by one of my supervisors [110]. Although this definition was very specific, it can be argued to be fair and necessary. When undertaking a review of reviews the data is an extra step away from the original research, and in order to be able to understand and critically appraise findings appropriately the reviews need to provide a minimum amount of methodological information in order to do this. Our definition for a systematic review aimed to ensure that included articles would be more likely to have this type of methodological information. The specific issues of quality assessment of included reviews will be addressed later in this chapter.

**Summary**

In summary, reflecting on the inclusion and exclusion criteria there were two potential alternative approaches that could have been adopted which might have achieved the original aims of this review more successfully. The first would have been to undertake a systematic review of the primary literature, or secondly to have applied less specific inclusion and exclusion criteria, in particular in this case there may have been a value in broadening the intervention type in order to provide an evidence based discussion on the merits of different types of interventions.

4.4.2.3 Quality assessment

Smith et al provide some guidance about undertaking quality appraisal, and based on their recommendation the AMSTAR score was used here [128].

Along with the Smith et al methods paper above, there is further guidance on methods for quality appraisal within the Cochrane handbook, where they advise that two different quality assessments are required; first the methodological quality of the reviews within the overview, and secondly a description of the quality of the evidence in these included reviews (Chapter 22, page 620) [131].
Using quality appraisal tools such as AMSTAR has been suggested as a way of systematically evaluating the methodological quality of a systematic review, with the potential to provide a cut off for eligibility for inclusion based on the score [128]. It has successfully been used in this way in a recent comprehensive overview of systematic reviews exploring asthma and dietary intake [136]. While Cochrane recommend the two different levels of quality appraisal are undertaken they do not go as far as to advise inclusion or exclusion based on quality appraisal, but rather using the assessment in formulating conclusions about the strength of evidence underpinning any findings. By their nature, Cochrane meta-reviews generally only include Cochrane systematic reviews, and therefore the information about quality of included primary studies is available. When undertaking a non-Cochrane meta-review many of the included reviews do not describe the quality of their included primary studies, as happened here, and it is how best to manage this situation that remains uncertain. The use of AMSTAR at least allows the lack of information about quality of included studies to be highlighted systematically, whether or not it is used as an inclusion criterion in its own right.

When we were planning this review originally in 2011, AMSTAR was a relatively new scoring system. Subsequent to our use of this scoring system it has been used by other research teams who have requested that the authors of AMSTAR ‘produces additional guidance for its’ application in order to improve its reliability and usefulness’ [137], a sentiment that seems worthy of support. They do now have a website (http://amstar.ca accessed 27/04/2016) which provides further guidance notes on their individual questions, and also states that they are in the process of developing an instrument called AMSTAR_NRS for assessing systematic reviews of non-randomised studies, which would be a welcome addition to the existing appraisal tools.

We investigated using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) as a different way of evaluating the quality of the systematic reviews [138]: the quality of the reporting within it, rather than the quality of the methodology. However, this was not easily used to provide an overall score, and was not readily adaptable to include the non-quantitative reviews.
Undertaking formal quality appraisal is a strength of this review, particularly given reports that it is frequently omitted [128]. Research by Pieper et al quantifies the scale of this problem, where they aimed to describe the methodological characteristics of published overviews of systematic reviews in their own systematic review published in 2012 [124]. They described 126 overviews and worryingly found that 1/3 did not provide any systematic quality appraisal of their included systematic reviews. Harling et al undertook a similar review also published in 2012, where they also aimed to describe the methodological approaches in overviews of interventions [130]. They reported that quality assessment was performed in 75% of the included overviews, and at least 9 different tools were used. Quality of the body of evidence was only undertaken in 17% of overviews. They conclude, along with Pieper et al, that there is a need for methodological rigour and consistency in overviews, along with reporting guidelines to improve the quality of this type of publication, a conclusion supported here [124, 130].

4.4.2.4 Presentation of results

Smith et al recommend that when presenting results from meta-reviews they should provide the major conclusions of the review (e.g. answer to the research question) as well as the evidence base for their conclusion, along with an assessment of the quality of the evidence for each conclusion [128]. This relies on included reviews providing an assessment of the quality of the body of evidence, and the absence of this is a major potential weakness for this method, and the absence of it in this review limits the conclusions that can be drawn.

4.4.2.5 Implications for practice and research

Smith et al highlight that an important role for this method is to help clinicians and policymakers to address the issue of understanding discordant reviews, and this is highlighted as an important role for this method elsewhere in the literature [124]. Exploration and understanding of the reasons for discordance between already published reviews can help clinicians and policy makers base decisions on the evidence most suitable to their own situation and can be considered a major strength of this method [124]. Unsurprisingly, Smith et al reiterate the importance of quality appraisal when aiming to provide useful
summaries that can inform clinical practice stating: “the strength of the conclusions and the ability to provide decision-makers with reliable information depends on the inclusion of reviews that meet a minimum standard of quality” (page 3) [128].

4.4.3 Comparison with the literature

Concern about methodological rigor is not limited to the newer method of meta-reviews. The article included here performed poorly on AMSTAR scoring, and the quality of reviews of reviews can only be as good as the included reviews. The meta-review presented in this thesis shows this is still problematic.

With regard to outcomes, Bussey-Smith et al [129] findings are comparable with other reviews in this area. The Cochrane systematic review by McLean et al in 2010, focussing on tele-healthcare in asthma, reported mixed findings but overall concluded there was no evidence of benefit in clinical outcomes [84]. However, they did suggest that there was possibly more of a role for those suffering more severe disease. One could speculate that the daily work involved with most tele-monitoring interventions is only considered worthwhile by those with more severe disease with ‘more to gain’. The same team considered tele-healthcare in chronic diseases including asthma [139] and found mixed results again, but importantly highlighted the importance of contextual factors such as the ability of the patients to interface with technology, an area of discussion missing from Bussey-Smith’s review. Importantly, there was no information about development of interventions and whether there had been any user testing involved, which is increasingly seen as an integral part of good quality intervention development [100].

The included study in this review (Bussey-Smith et al) did not address the issue of adverse events when using digital interventions to support self-management, and a recent systematic review published in 2014 reports the lack of systematic reviews addressing adverse events is a key gap in the literature [8]. Those few reviews which have addressed adverse events suggest that while there is no evidence of control groups having better clinical outcomes, a higher rate of dysphonia or oral candidiasis in intervention groups has been noted in effective interventions [84, 140]. This side-effect is related to higher doses of, or better
adherence to, inhaled corticosteroids, which itself is a positive outcome. Surprisingly, the issue of patient satisfaction also appears neglected in published literature. Morrison et al [8] only found one systematic review reporting patient satisfaction [84], where they reported participants preferred a web-based system to a paper based one.

Descriptions of intervention development and particularly the use of theory has been shown to increase effectiveness of behaviour change interventions [141] and the importance of reporting this information about development processes (e.g. the degree of user testing, and the use of theory to inform content) has been further highlighted by the publication of a CONSORT EHEALTH statement which includes it [16]. Bussey-Smith et al made no mention of theory during development of the included interventions, and made no attempt to collect or report that data [129]. Given that Bussey Smith et al was published in 2007 [129], it could be speculated that it was not until the MRC Framework was updated in 2008 [100] that the importance of reporting this aspect of development gained further prominence. There is encouraging evidence that more recent studies are more likely to provide this extended information, facilitated by the increasing availability of online appendices and less stringent word counts in journals [8]. Another reason for increasing emphasis on using theory during development is the increasingly widespread uptake of the behaviour change taxonomy [107], described in more detail in Chapter 3. This taxonomy brings behaviour change theory to a wider audience than it previously experienced.

What appears consistent across several systematic reviews on digital support for self-management of chronic illness in general is that interventions with multiple behaviour change techniques appear, on the whole, to be more effective than those using fewer, and that the use of theory to inform the choice and combination of BCTs appears to be associated with increasing effectiveness of the interventions [14, 141, 142]. The meta-review presented in this thesis was unable to provide any results on this topic.

Dropout rates were summarised by Bussey-Smith [129] as ranging from 0% to 31%. This is in keeping with other systematic reviews of digital interventions in other areas, for example a recent Cochrane review examining computer based
weight loss interventions found attrition rates ranging from 2-25% (median 16%) [143], and attrition may be worse in interventions targeting older age groups, with one review including digital and non-digital interventions noting rates between 0 and 52% (median 15%) [142]. Reassuringly attrition rates are no worse than those found with non-digital self-management asthma interventions as described in Gibson’s Cochrane review examining asthma self-management education and regular health professional review, where attrition rates ranged from 0% to 54% (median 15%) [6].

Only one of the included studies had a follow up period of more than 12 months (Bartholomew went up to 15.6 months although the mean was 7.6). Therefore, it is difficult to draw conclusions about sustained benefits in knowledge and symptom scores. Since Bussey Smith published their review in 2007 [129] several other digital interventions have been trialled. These are described in detail in Chapter 7, but one worth mentioning here is the van der Meer study of a digital intervention to support self-management as it is the only one to date to provide additional follow up results [94]. They have now published data looking at participants 1.5 years after losing access to the intervention. Encouragingly this has shown sustained benefits in the intervention group in asthma control questionnaire and asthma quality of life scores, providing hope that there is scope for a sustained benefit with such digital interventions [144].

4.4.4 Answering the research question

This review provides some evidence about the effectiveness of digital interventions, but little data about what helped or hinders their uptake with participants. In order to understand how the literature could help inform the content of the intervention being developed within this thesis it was necessary to undertake a subsequent literature review focussing on barriers to adherence, a background search of the literature for advice about what were considered to be essential features of any asthma self-management intervention (Chapter 2), and a literature review of primary studies featuring interactive interventions aimed at adults with asthma (reported in Chapter 7), to allow comparison with that subsequently developed and evaluated here as described in chapters 5 and 6.
4.4.5 Conclusion

This meta-review found only one poor quality systematic review featuring digital interventions to support self-management of asthma. When using systematic review of systematic review methods careful consideration is required to ensure inclusion and exclusion criteria are broad enough to provide articles meeting inclusion criteria. Alternatively, if maintaining the narrow scope is important then a review of the primary literature may be more appropriate. The main conclusion from this meta-review was that further robust investigation is needed firstly in the form of a detailed primary systematic review of published digital interventions aimed at those with asthma, ideally detailing the presence or absence of BCTs. Such a review has subsequently been undertaken in my department and is currently in press as of April 2016 [145]. To a large extent this also demonstrates that further more robust investigation is merited. Secondly, examination of the primary qualitative literature to describe what is already known about the patient’s perspective would be invaluable to inform future interventions, and I am aware that Prof Lucy Yardley’s team in Southampton are currently undertaking a systematic review of barriers to uptake and use of self-management interventions in asthma - the findings of which will be very relevant to this PhD.
Chapter 5: Development of the Living Well with Asthma Website

5.1 Introduction & aims

This chapter details the methods, results, and discussion from the second stage of my PhD project: developing the “Living Well with Asthma” website. The overall aim of this stage is to describe the collaborative development of an online asthma self-management intervention, produced iteratively using feedback from potential end users, resulting in an intervention ready to be evaluated by patients within a pilot RCT, the methods and results of which are presented in the following chapter.

5.1.1 Contributors: The expert panel

I recognised at the earliest planning stages of this project that I needed input from researchers with specific experience of developing digital interventions. With my PhD supervisors, I convened an ‘expert panel’ who would provide advice during this stage. The expert panel are listed in Table 5.1.
Table 5.1 Living Well with Asthma expert panel

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
<th>Expertise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prof Frances Mair</td>
<td>Professor of Primary Care Research University of Glasgow</td>
<td>PhD Supervisor. Expertise in evaluating and implementing complex interventions. Expert in implementation theory.</td>
</tr>
<tr>
<td>Prof Sally Wyke</td>
<td>Interdisciplinary Professor of Health and Wellbeing University of Glasgow</td>
<td>PhD Supervisor. Expertise in behaviour change, self-management intervention development and evaluation.</td>
</tr>
<tr>
<td>Prof Neil C Thomson</td>
<td>Professor of Respiratory Medicine University of Glasgow</td>
<td>PhD Supervisor. Expertise in asthma management and clinical trials.</td>
</tr>
<tr>
<td>Dr Marilyn McGee-Lennon</td>
<td>Senior Lecturer in Computing and Information Sciences University of Strathclyde</td>
<td>Expertise in Human-Computer Interactions, and digital intervention development and testing.</td>
</tr>
<tr>
<td>Prof Lucy Yardley</td>
<td>Professor of Health Psychology University of Southampton</td>
<td>Expertise in behaviour change theory, and developing and evaluating behaviour change interventions. Co-developer of LifeGuide software (used in this project).</td>
</tr>
<tr>
<td>Prof Mike Thomas</td>
<td>Professor of Primary Care Research University of Southampton</td>
<td>Expertise in asthma self-management, and evaluating interventions. Medical director with Asthma UK.</td>
</tr>
<tr>
<td>Dr Deborah Morrison</td>
<td>Clinical Academic Fellow University of Glasgow</td>
<td>PHD student. General Practitioner with interest in asthma and self-management.</td>
</tr>
</tbody>
</table>

5.2 Methods

5.2.1 Rationale for methods used

Much of this has already been discussed in chapter 3, which makes it clear how central the MRC guidance on the development and evaluation of complex interventions was to this projects methodology [100]. In particular, the following statement from this guidance was integral to my plans for how this phase would progress:

“Developing, piloting, evaluating, reporting and implementing a complex intervention can be a lengthy process. All of the stages are important, and too strong a focus on the main evaluation, to the neglect of adequate development and piloting work, or proper consideration of the practical issues of implementation, will result in weaker interventions, that are harder to evaluate, less likely to be implemented and less likely to be worth implementing.” Pg 4.

As shown previously in Chapter 3, the illustration of the process is shown again in Figure 5.1, which shows the key stages recommended when developing a complex intervention, with the ‘Development’ element circled below particularly relevant to this chapter.
What is not clear from Figure 5.1 is the importance the MRC guidance places on user involvement during planning and development of complex interventions. In response to this guidance, and advice from the expert panel, I undertook focus group discussions and think aloud studies as methods of co-designing the intervention with potential end users, as explained earlier in chapter 3. Think aloud studies involve asking users to vocalise their reactions and thinking processes in real-time while using the online resource (or preceding prototype materials) [32, 146, 147] and are considered an essential step when developing any type of website [116]. These think aloud studies are described in full in the relevant sections below.

As seen from the quote from the MRC guidance the consideration of implementation issues is advised at the earliest of stages. In order to fulfil this requirement I chose to use Normalisation Process Theory (NPT), as I have used this in other projects previously [45, 46, 148], and as described in Chapter 3 it can be valuable even at the earliest stages of complex intervention design [101, 111]. NPT is increasingly seen as a means to understand implementation processes and enhance the implementability of interventions [109, 111]. So, while it did not directly influence the specific contents of the website, it was used to guide our co-design methods, consider long-term implementation issues of the intervention itself, and also as described in the next chapter to analyze our trial procedures to ensure the evaluation itself was feasible.
5.2.1.1 Choice of software

I used LifeGuide software to develop this intervention. Traditionally, development of online behaviour change interventions would be very resource intensive with each intervention requiring to be programmed individually by a team of programmers from scratch. The cost involved in this would have rendered this project, and many like it, unworkable. A team based at Southampton University recognised this barrier to developing digital interventions and in response have developed an open access software package called LifeGuide, funded by the Economic and Social Research Council [118, 119]. LifeGuide allows researchers with no computer programming experience, like myself, to easily and flexibly create internet-delivered interventions. It has been used successfully in a number of health related interventions [42, 119, 149, 150].

The LifeGuide software consists of 3 parts[151]:

1) an authoring tool which is used to create the pages of an intervention, such as text, videos, images and questionnaires.

2) The logic which is a written set of commands that works behind the scenes of an intervention to make it run as expected.

3) an intervention manager, which is a server to run the intervention. This allows the information that users enter into the website to be stored securely, then downloaded for analysis as required. It also tracks participant usage of an intervention, page by page.

A key design feature of LifeGuide is that researchers can easily test parts of an intervention and immediately modify and improve it based on the findings. This makes user testing during the development phase easier and efficient, a feature which should, as reported by the MRC guidance, increase the likelihood that an intervention can, and should be implemented in the longer term [100].
5.2.2 Methods overview

In chapter 3, I outlined the rationale for the choices of the methods used. This section describes what I actually did. Here, I describe the two phases of work I undertook to incorporate the processes recommended by the MRC. As Figure 5.2 illustrates, this process is not linear, with various steps occurring in parallel with iterative incremental progress at different phases happening simultaneously.

Phase 1 describes the intervention planning, and completion of a low fidelity (draft) version of the website and phase 2 describes the processes involved in taking the low fidelity prototype and converting it into a finished website ready for evaluation in a randomised controlled trial (RCT). This is shown visually in Figure 5.2.

Figure 5.2 Overview of stage 2.

5.2.2.1 Ethics and management approvals for user testing (focus groups and think aloud studies)

Ethical approval was granted from the West of Scotland Research Ethics Committee (REC)(12/WS/0068) and management approval from NHS Greater Glasgow and Clyde (GN11RM394) in March 2012. I applied using a new system
that was being piloted called ‘proportionate review’. This alternative process is for studies with ‘non material ethical issues’, e.g. studies that have minimal risk, burden or intrusion for research participants, and includes non-sensitive questionnaire and interview studies. This expedited process meant no attendance at a REC panel meeting, and a decision made within 2 weeks of applying.

There was a separate study information leaflet for adults with asthma (appendix 7) and practices nurses (appendix 8). Prior to providing written, informed consent, all participants had at least 24 hours (usually longer) to review the material and had opportunity to ask questions.

5.2.2.2 Data Storage & Confidentiality

Data was stored electronically in password protected files on the secure university server. Audio tapes/digital recorders, consent forms and field notes were kept in secure locked cabinets. Importantly, there was no requirement for me to access medical records for patient information, as medications and health contacts were self-reported. Identifiable data will be securely kept for 5 years after the conclusion of the study, and anonymised research data for 10 years. I followed the Caldicott principles at all times.

5.2.2.3 Participants

In the co-design stages we were aiming to include both those who might use the intervention themselves (e.g. adults with asthma); and the health professionals who might recommend it. In a UK setting, this would be primary care practice nurses, who undertake asthma reviews. Having heterogeneous focus groups is not always recommended [152] but in this situation I was particularly interested in understanding the disparity between what practice nurses recommend to adults with asthma, and what the patients actually do in real life, therefore this was appropriate.

Recruitment to the focus groups and think aloud studies was undertaken simultaneously. Practice nurses were recruited via snowballing and word of mouth. When recruiting for adults with asthma I used a range of sources: primary care, Asthma UK Research and Policy volunteers, Chest Heart Stroke
Scotland volunteers and a secondary care asthma clinic at Gartnavel General Hospital. I also put up posters around the University of Glasgow, and two local hospitals (Western Infirmary and Gartnavel General). Potential participants could consent to take part in a focus group, up to two think aloud studies (described in phase 2), or both. Practice nurses were only eligible for focus groups. I was aiming to include 4 to 6 adults with asthma and 2 to 4 practice nurses per group (e.g. minimum of 6 per group), and planning a maximum of 12 think aloud studies. All participants were provided with a gift voucher to compensate them for their time, and allowed to claim travel expenses.

5.2.2.4 Inclusion and exclusion criteria

For adults with asthma:

Inclusion Criteria:

1. diagnosis of asthma
2. using any inhaled medication for their asthma on average twice a month or more often
3. age 18 or over

Exclusion criteria:

1. a history of mental impairment that would suggest that they would be unable to give informed consent to participate
2. a history of hearing or speech impairment to a degree that would render normal conversation impossible
3. unable to speak English well enough for normal conversation
4. a terminal illness

The only requirement for practice nurses was that they had to be regularly undertaking asthma reviews with patients in GP surgeries.

5.2.3 Phase 1 Methods: Intervention planning

Phase 1 describes the process of developing a ‘first draft’ of the website. This phase consisted of three main work packages (WP), all overseen by the expert panel.
5.2.3.1 Work package 1 – Understanding the evidence & incorporating theory (scoping review and expert panel)

Campbell et al [115] recommend working through 5 key tasks when planning a complex intervention, in order to define and understand the ‘problem’ that your intervention is aiming to solve. These 5 tasks are:

1. defining and quantifying the problem;
2. identifying who is mostly likely to benefit;
3. understanding the pathways which contribute to the problem;
4. consideration of whether (and how) these pathways are amenable to change;
5. and attempting to quantify the potential for improvement.

The results from Chapter 2, and the experience of our expert panel, was drawn on to complete these tasks. In addition to using the literature to complete the 5 tasks described above, I also used it to directly influence the specific content of the resource. I did this by scanning relevant articles from the literature (including asthma guidelines) and extracting any statement which could be seen to be a barrier or facilitator to good asthma control and self-management, and any statement which described the ideal contents of a self-management intervention (digital or otherwise), as outlined at the end of chapter 2.

5.2.3.2 Work package 2 – Getting user perspectives on a web resource (focus groups)

In order to investigate the credibility of this list with potential end users I convened 2 focus groups, consisting in total of 9 adults with asthma (6 female, 3 male), and 4 practice nurses who undertake asthma reviews. Focus groups were held at the Department of General Practice & Primary Care, University of Glasgow, and were audio recorded and transcribed.

NPT [111] was used to inform the topic guide for these focus groups. NPT aims to explain the routine embedding of practices by reference to the role of four constructs: coherence; cognitive participation; collective action and reflexive monitoring.
• Coherence: refers to the work of making a complex intervention hold together and cohere to its context, how people “make sense” or not of the new ways of working.

• Cognitive participation: is the work of engaging and legitimising a complex intervention, exploring whether participants buy into and/or sustain the intervention.

• Collective action: examines how innovations help or hinder professionals in performing various aspects of their work, issues of resource allocation, infrastructure and policy, how workload and training needs are affected and how the new practices affect confidence in the safety or security of new ways of working.

• Reflexive monitoring: is the work of understanding and evaluating a complex intervention in practice, and how individuals or groups come to decide whether the new ways of working are worth sustaining.

These constructs are applicable regardless of whether its use is at the stage of developing a complex intervention such as here, during development of an intervention, optimising trial parameters, or the actual implementation of complex interventions [111].

Therefore, NPT provides a conceptual framework to help clinicians, researchers and managers describe and potentially to judge the implementation potential of an intervention, either allowing for improvement and development prior to implementation, or if required an acceptance that the intervention simply lacks implementability and that further work is not warranted.

The full topic guide is available as appendix 9, and summarised in Table 5.2
### Table 5.2 Summary of how NPT informed focus group topic guide

<table>
<thead>
<tr>
<th>NPT Construct</th>
<th>Construct explanation</th>
<th>Focus group guide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coherence</td>
<td>Meaning and sense making by participants</td>
<td>Explore perspectives on the information presented (from the literature review), and views on the potential role of an online resource</td>
</tr>
<tr>
<td>Cognitive participation</td>
<td>Commitment and engagement of participants</td>
<td>Discover potential users’ views of the idea of an online self-management website including barriers and facilitators to utilisation.</td>
</tr>
<tr>
<td>Collective action</td>
<td>The work participants do to make the intervention function</td>
<td>Investigate what people currently do to manage their asthma, and what role an online resource might have.</td>
</tr>
<tr>
<td>Reflexive monitoring</td>
<td>Participants reflect on or appraise the intervention</td>
<td>Discover what participants would like to see, that ensures the intervention is helpful, and worth using.</td>
</tr>
</tbody>
</table>

The focus groups were transcribed. I intended to use NPT to inform the analysis of the focus groups, and initiated a coding frame based on NPT. However, in practice I realised that comments could be essentially distilled down into either barriers or facilitators to self-management or suggested features. Therefore, I simply extracted statements which fell into one of these categories and used this to develop a list of features a website should ideally include.

#### 5.2.3.3 Work package 3 – Developing a draft version of the website (expert panel)

The list of suggested features to include in the website generated by WP 1 and 2 was reviewed and by the expert panel and an agreed list finalised. I generated low fidelity prototype pages, initially using Microsoft Word or PowerPoint (also referred to as draft pages) to cover all the topics in our agreed features list. These draft pages were reviewed initially by those in the panel with a clinical background to ensure the content was factually correct. Subsequently the pages were shown to members of the expert panel with specific expertise in behaviour change theory to ensure maximum opportunity for promoting behaviour change was incorporated into each page or section. From this a draft version of each potential webpage was finalised, ready for think aloud study evaluation.
5.2.4 Phase 2 methods: Iterative refinement of the resource contents of the website (think aloud studies and expert panel)

Draft pages developed during phase 1 were gradually translated into interactive webpages, with input from potential end users in the form of think aloud studies, and ongoing review by the expert panel. I undertook think aloud studies at either the participant’s home, or the Department of General Practice & Primary Care, University of Glasgow, depending on participant preference. There were two waves of think aloud studies: the first 4 used draft webpages consisting of mainly paper or PowerPoint slides, the latter 6 were mainly undertaken using the prototype webpages on LifeGuide. While LifeGuide can be used by researchers with no computing science background, due to time constraints Andrew Ramsay a computer science researcher transferred the majority of the draft pages into LifeGuide initially. I introduced these initial think aloud tasks by explaining that the website was at an early stage of development, and therefore there was much scope for modifying the contents and that critical comments were the most helpful. Participants were asked to say whatever they thought or felt about what they were seeing, with prompts and questions used to elaborate on responses. The participants were then encouraged to voice any additional suggestions or opinions to improve the resource, for example what they liked and disliked, what was intuitive and what was not, and how they envisaged using such a website in real life in the future.

During the first few think aloud studies the emphasis was on the content of the website. I used mainly Microsoft Word documents or PowerPoint to show ideas for potential pages. For example the ‘Common concerns and queries’ section initially consisted of a word document with a list of questions and I had sample answers on separate slips of paper. I asked users to ‘press’ the relevant question they were interested in, and I presented the relevant slip of paper with the suggested answer. Although rudimentary, this allowed an early appreciation of how this section would work in practice, and how it could be improved.

Once pages were on the LifeGuide software they were given a unique name (page_2_2, page_2_3, etc), which was noted as each new page was viewed to allow correlation between a specific website page and what was recorded during the think aloud study. For example page_2_2 corresponded to section 2
(treatments), page 2. As well as digital audio recordings, I kept written notes of the issues raised that would directly impact on the website development, page by page. Areas requiring rewritten, typographical errors, and suggestions for improvements were all noted this way, allowing me to actually go ahead and make the required changes usually within 24 hours, and in the majority of cases before the next think aloud study. The only exception to this was when two think aloud studies were held on the same day. At times, this was helpful to quickly get two opinions in quick succession about a specific page or idea, to allow me to decide how to proceed.

I also thematically analysed the transcribed think aloud studies, with the aim of providing information for further development of the resource following the pilot RCT. NPT was not used for analysing the transcribed think alouds studies, as the majority of comments were very ‘practical’ in nature, and page specific rather than about the intervention itself. A coding frame was developed from reading through the first three studies (Figure 5.4). SW and I both independently coded the first two transcripts, and compared our results, after which I coded the remaining transcripts. Comments were also noted to be either:

1) A positive comment, where the user liked or identified with what they saw.
2) A negative comment where the user disliked or disagreed with what they saw.
3) Where the user suggested an improvement or alternative way of presenting the data.

Towards the end of this phase, I made links with other health professionals based in the local health board with an interest in asthma self-management i.e. primary care practice nurses, secondary care respiratory nurses, and respiratory pharmacists. This was to ensure that the website was consistent with health professionals’ usual advice to patients, and to establish informally if they had suggestions for improving it.

The final version of the Living well with Asthma website was formally mapped to Michie and colleagues latest behaviour change technique (BCT) taxonomy [107]
in order to describe which BCTs were present. There are 93 individual BCTs, which can be grouped into 16 different BCT areas. To map the BCTs I reviewed every page of the website and where relevant assigned a BCT. These were all subsequently reviewed by SW, and discrepancies discussed until we both agreed. We did this to provide a reliable record of the content of this behaviour change intervention, and to confirm that I included a range of BCTs as planned.

Throughout both phase 1 and 2, I iteratively undertook ‘NPT analysis’ of the intervention as it was being developed in order to enhance the likelihood that what we were developing would be implementable long term [111].

5.3 Results

This section describes the results of the two phases of work that were undertaken to develop the website and illustrates the iterative nature of the website development. Phase 1 describes the initial planning and deciding what the content should be, and phase 2 describes how this planned content was converted into interactive webpages.

5.3.1 Phase 1 results: Initial planning

5.3.1.1 Work package 1 – Understanding the evidence & incorporating theory (literature review and expert panel)

The planning stage had two outcomes: firstly I focused on the 5 key tasks outlined by Campbell et al [115], and secondly I generated a list of potential features the website might contain. The 5 tasks were completed using a combination of existing published literature including guidelines, along with input from the expert panel. The literature was used inform the completion of these tasks, as outlined in turn below.

Task 1: Define and quantify the problem

A review of the asthma literature over the last 15 years in particular makes it clear that when optimum self-management of asthma is undertaken it improves a range of asthma outcomes (fewer visits to emergency room, hospitalisations, unscheduled visits to doctors, and days off work and school, reduces nocturnal asthma and improves quality of life) [6]. As outlined in more detail in Chapter
2, optimum self-management of asthma means regular health professional review and good self-management education including agreeing an asthma action plan (AAP) [6]. Unfortunately, in real life settings it is an underused treatment strategy, particularly the use of AAPs. This is evidenced by:

1. Suboptimal use of preventative therapies. Adherence to therapies in long term conditions is around 50% [153], and as low as 30% in asthma [154]. Low use of preventative inhaled corticosteroids (ICS) therapies and high use of short acting beta agonists (SABA), also called reliever inhalers, is a pattern commonly seen, and which is associated with poorer asthma control [2].

2. High levels of symptom burden (46% daytime symptoms and 30% nocturnal symptoms) [39], with lack of recognition of scope for improvement: 50% of patients reporting severe persistent symptoms report their own asthma as being completely or well controlled [39]. This results in people with uncontrolled or deteriorating asthma not seeking timely medical advice.

3. Suboptimal attendance at asthma reviews with low use of asthma action plans (AAPs) [1, 10] as verified by the National Review of Asthma Deaths (NRAD) where only 23% of those who died having been provided with an AAP [1], and attendance at asthma reviews in Scotland were only 65%.

Task 2: Identify and quantify the population most affected, most at risk, or most likely to benefit from the intervention

The Global Initiative for Asthma (GINA) guidelines were used particularly for this task as they list the risk factors for poor asthma outcomes [7]. These are:

- Uncontrolled asthma symptoms
- Increased use of short acting beta agonist e.g. reliever therapy
- Inadequate inhaled corticosteroids, including poor technique.
- Low FEV\(_1\) (especially if <60% predicted)
- Major psychological or socioeconomic problems
- Smoking
- Comorbidities: obesity, rhino-sinusitis, food allergy
- Previous exacerbations or intensive care admissions for asthma
The majority of these factors are directly related to uncontrolled asthma symptoms, and therefore we agreed a key way of identifying those most likely to benefit from a self-management intervention is to target those with uncontrolled asthma symptoms. There are widely used validated questionnaires which can easily define individuals as being uncontrolled, for example the asthma control questionnaire [155].

Task 3: Understand the pathways by which the problem is caused

With reference to problems outlined in Task 1, the literature and guidelines provided explanations for why these problems are sustained, is correspondingly shown below:

1. Reasons for low adherence to asthma therapies are often related to concerns about side effects, or perceptions that they do not need to be on treatments [59, 156].
2. The global asthma insights and reality surveys [2] provides evidence of suboptimal asthma control and suggests reasons for it. First, people with asthma overestimate how controlled their asthma is, therefore do not consider themselves to be candidates for gaining improvement with asthma treatments [2, 41]. Second, those who do acknowledge they have symptoms and limitation of activities accept them as unavoidable consequences of having asthma, rather than seeing the potential for improvement [2, 41].
3. Patients’ reasons for not attending asthma reviews revolve around feelings that their asthma is not serious enough [157]. AAPs are underused for several reasons as determined by Ring et al in their systematic review [9]:
   a. Differences in beliefs and attitudes between health care professionals and people with asthma.
   b. Perceived irrelevance of AAPs of the part of those who would potentially benefit from them
   c. Health professionals only offer AAPs to select groups of patients (e.g. with well controlled asthma, or those with higher levels of educational achievement).
In summary, people with asthma often underestimate their symptoms and overestimate their control, not making use of available therapeutic options (medications, AAPs and advice from health professionals). Those who do recognise they have symptoms may not adhere to prescribed medications due to misunderstandings around medication side effects, or perceived benefits of using AAPs.

**Task 4: Explore whether these pathways may be amenable to change and, if so, at which points**

Again with specific reference to the three ‘problems’ outlined in Task 1, I derived strategies which would aim to overcome the problems identified in task 1, aiming to include behaviour change techniques (BCTs) [107] where possible, targeting the underlying mechanisms as explained in Task 3. These strategies were:

1. Prompting users to consider reasons why they do not take medications regularly (barriers) and consider strategies to overcome these barriers. Providing information about benefits of inhaled corticosteroids, challenging misconceptions and negative beliefs. Focussing on benefits meaningful to individuals such as fewer days off work, managing that exercise class etc. Providing instructions (ideally including videos) to demonstrate correct inhaler technique.

2. Promoting the message that users should be aiming for no symptoms. Providing information to challenge the belief that having asthma symptoms is normal, and asking validated questions to determine if users are currently putting up with symptoms, providing feedback on response. Prompting users to recognise if they avoid activities due to their asthma, or are limited in everyday tasks such as housework, gardening, visiting friends. Turn these limitations into ‘goals’ to aim towards, and describing how these goals are achievable for them.

3. Provide information that people who use AAPs and attend for reviews have fewer symptoms and fewer asthma attacks. Provide quotes from practice nurses encouraging attendance for reviews. Remove physical barrier to using AAPs by providing a template that can be taken to health professionals (identical to those provided by local health board).
The expert panel ensured that behaviour change theory was incorporated into the web page contents and full analysis of behaviour change techniques present was undertaken on the final website [107].

**Task 5: Quantify the potential for improvement**

The literature provided the information for this task. An estimated 300 million people worldwide have asthma and its prevalence appears to be increasing with an estimated additional 100 million people with asthma by 2025 [37]. Depending on criteria used to define poor control, evidence suggests that levels of uncontrolled asthma range from at least 25%, but are probably higher [2, 11, 39]. My primary outcomes if this intervention was subsequently taken to a full scale RCT would be to assess symptom level using a questionnaire. A good candidate would be the Asthma Control Questionnaire (ACQ) and we would aim for a drop of 0.5 in score, which is the minimally important clinical difference [158]. Symptoms was the most commonly described outcome in my previous metareview of digital interventions reported in 12 out of 19 of the RCTs [8].

**Literature review**

In addition to using the literature to complete the 5 key tasks it was also used to directly inform the specific contents of the website. At this stage this was used mainly to develop a list of barriers and facilitators to asthma self-management. How this list actually informed the content is fully described at the end of work package 2, section 5.3.1.2 below.

**5.3.1.2 Work package 2: Getting user perspectives on a web resource (focus groups)**

We shared the key findings from Tasks 1 to 4 above, and our list from the literature, with potential end users in the focus groups. Excluding the practice nurses the average age of participants was 42 years (range 23 to 56). Six participants were female, 4 male, and included participants from highest and lowest deprivation deciles (median 4, IQR 1, 8). Table 5.3 describes the participants, illustrating which focus group (or think aloud study) they participated in. Achieving participant numbers was relatively quick, however the asthma UK research volunteers responded most quickly, and this led to half of the participants being recruited this way. Recruitment was stopped once we
had enough members to hold the 2 focus groups. I then intended a second wave from primary care if I needed further participants for the think aloud studies, however I was able to recruit for them from the pool of participants who had responded to the initial mailing. Overall, participants were recruited from Asthma UK volunteers (n=5), primary care (n = 3) and hospital asthma clinic (n=2), with none recruited via poster. All 4 practice nurses were female and had been nursing for an average of 25.5 years (range 21 - 30), and undertaking specific primary care asthma reviews for on average 7.7 years (range 5-10). As described in the methods section NPT was used to inform the development of the focus group topic guide. This was useful as it encouraged me to consider a range of questions I would not have done otherwise. For example, we planned to ask what features would be in the ideal self-management resource. NPT then ensured that relevant exploratory questions were asked about how that feature would work in practice, who would use it, and would someone really be likely to sustain its use in the long term.
Table 5.3 Demographics of participants in focus groups and think aloud studies

<table>
<thead>
<tr>
<th>Participant number</th>
<th>FG 1</th>
<th>FG 2</th>
<th>TA 1 #</th>
<th>TA 2 #</th>
<th>Female</th>
<th>Years since diagnosis</th>
<th>Age (yrs)</th>
<th>SIMD §</th>
<th>Ethnicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>●</td>
<td>●</td>
<td>(2)</td>
<td>●</td>
<td>7</td>
<td>44</td>
<td>1</td>
<td>White British</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>●</td>
<td>●</td>
<td>(3)</td>
<td>●</td>
<td>9</td>
<td>23</td>
<td>1</td>
<td>White British</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>●</td>
<td>●</td>
<td>(4)</td>
<td>● (11)</td>
<td>50</td>
<td>51</td>
<td>8</td>
<td>White British</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>●</td>
<td>●</td>
<td>(5)</td>
<td>● (9)</td>
<td>40</td>
<td>46</td>
<td>4</td>
<td>White British</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>●</td>
<td>●</td>
<td>(6)</td>
<td>●</td>
<td>12</td>
<td>23</td>
<td>1</td>
<td>White British</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>●</td>
<td>●</td>
<td>(7)</td>
<td>●</td>
<td>31</td>
<td>56</td>
<td>8</td>
<td>White British</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>●</td>
<td>●</td>
<td>(8)</td>
<td>●</td>
<td>19</td>
<td>55</td>
<td>3</td>
<td>White British</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>●</td>
<td>●</td>
<td></td>
<td>●</td>
<td>34</td>
<td>41</td>
<td>6</td>
<td>White British</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>●</td>
<td>●</td>
<td></td>
<td>●</td>
<td>28</td>
<td>29</td>
<td>10</td>
<td>White British</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>●</td>
<td>●</td>
<td>(1)</td>
<td>(10)</td>
<td>9</td>
<td>48</td>
<td>10</td>
<td>White British</td>
<td></td>
</tr>
</tbody>
</table>

† Refers to adults with asthma participating. Participants recruited from: AsthmaUK (1,3,5,7,9); primary care (2,4,10); asthma clinic (6,8). Two practice nurses also present in each focus group, details not provided.

# Number in brackets refers to think aloud (TA) study number, participant number 3, 4 and 10 participated in two think aloud studies each.

§ Scottish Index of Multiple Deprivation. Range from 1 (most deprived) to 10 (most affluent)
During the first focus group it became clear that questions informed by the final construct - reflexive monitoring - were met with particular difficulty by the participants. It proved difficult for participants to imagine what would be evidence that a resource which they had not seen, or experienced themselves, was working for them. The other issue that became apparent during the focus group was that separating the work of asthma symptoms, asthma self-management, and then asthma self-management using a new website was difficult, not only for the participants but also for me facilitating the focus group. It was hard to steer participants away from their experiences of asthma symptoms, particular with one member of the group who had very severe asthma. In addition while the participants had lots of ideas about what should be in the resource (coherence), they were less clear about what would encourage commitment to undertaking these processes and engaging with a resource (cognitive participation) which is the domain I was particularly interested. One example of this was the issue of ‘putting up with symptoms’ and it was clear this was a key area that the website should focus on, and challenging people to not put up with symptoms was key strategy to use, but practical strategies to do this were not forthcoming.

When I reviewed the transcription of the first focus group I intended to use NPT for the analysis. I initiated developing a NPT based coding frame while reviewing this first transcript. This helped me realise that too much time was being spent on the users illness burden, and the treatment burden that those with severe asthma in the group experienced. In light of this I approached the second focus group differently. I steered participants towards a more forward looking ‘what could we do better’ discussion, rather than looking at what has not gone so well in their past. We explored more about why people put up with symptoms, and why people do not take their inhalers as prescribed. I asked more about tools to help people manage their asthma better, what would they like to see, beyond simply information. I started trying to code this transcript using NPT. However, when I only considered comments which were directly related to my research question (“What are the barriers and facilitators to the uptake and utilisation of a web based self-management tool from the perspective of adults with asthma, and primary care nurses who undertake asthma reviews?”) it became clear that the information provided from the focus
groups fell mainly into 2 categories: barriers to self-management (using digital resources or otherwise), and facilitators to self-management. Therefore, it made sense to simply group the statements into these two categories, rather than use NPT as planned.

Barriers to optimum self-management identified by focus groups included:

- not accepting diagnosis
- concerns about side-effects of medications
- difficulties keeping track of medications and remembering to order more
- the length of time between asthma reviews resulting in knowledge loss.

Facilitators to using an online resource included

- staggering of information
- a resource to bridge the gap between annual reviews and reinforcement of material covered in the review
- provision of email reminders i.e. ordering medication and flu vaccinations
- resource being promoted during annual reviews
- making users aware of different types of inhalers available and importance of finding one that suits.

One area of discussion in both groups was whether online forums should be provided in the website. Participants who had used currently available online forums had mixed views on them, often initially finding them useful and then subsequently becoming irritated with others users’ contributions. They did however recommend them overall, as is consistent with research in this area [159], and suggested we include them in our resource. However, I had previously discussed online forums with the expert panel and we had agreed the need for monitoring of forums simply meant they were beyond the scope of this project. In addition, Asthma UK has a popular and well used forum so it was unnecessary to duplicate this in our resource. It was useful to have decided this before the focus group as I was able to move on to more relevant topics by explaining this.
The barriers and facilitators to good self-management identified from the focus groups were combined with those from the literature (including asthma guidelines). Each individual barrier/facilitator statement was then assigned a potential website feature. While this full process is shown in appendix 10 (intervention planning document) an example is shown below in Table 5.4. Once the process was completed the intervention features were then grouped together, providing an evidence based rationale for the inclusion of each feature.

Table 5.4 Example of literature directly informing proposed website contents

<table>
<thead>
<tr>
<th>Barriers from asthma literature</th>
<th>Suggested intervention component</th>
</tr>
</thead>
<tbody>
<tr>
<td>People with asthma overestimate their control and tolerate unnecessary symptoms [2].</td>
<td>Provide tool to assess control/symptoms e.g. ACT, ACQ, or RCP 3 Questions.</td>
</tr>
<tr>
<td>Health professionals do not always offer AAPs to patients [10, 69, 70].</td>
<td>Provide alternative means of accessing AAP via freely available website, and promote users proactively approaching health professional about them.</td>
</tr>
<tr>
<td>People with asthma with a new diagnosis lacked confidence in using AAPs [70].</td>
<td>Provide information about how to use AAPs. Illustrate benefits &amp; low risk of harms. Provide examples of using AAP use, quotes aiming to increase confidence.</td>
</tr>
<tr>
<td>People with asthmas beliefs about medications can impact on adherence (E.g. effectiveness, tolerance, fears of side-effects) [40, 160].</td>
<td>Provide information to challenge beliefs: both facts and example experiences.</td>
</tr>
<tr>
<td>Impaired literacy is associated with reduced asthma knowledge and improper inhaler use [161], reduced aural literacy is associated with poorer asthma control measured by nights with symptoms [29].</td>
<td>Provide information in a graded way, where user can determine depth of information required. Use images, videos where possible.</td>
</tr>
</tbody>
</table>

ACT = Asthma control test, ACQ = Asthma control questionnaire, AAP = asthma action plan

5.3.1.3 Work package 3 –Developing a draft version of the website (expert panel)

WP 1 and 2 provided evidence for targeting six main behaviours. These were:

1. Recognise symptoms, do not put up with them (aim for no symptoms)
2. Optimise medication use (including inhaler technique)
3. Attend for regular asthma review
4. Use asthma action plans
5. Increase physical activity
6. Stop smoking
As outlined in Chapter 3, I needed to understand what we were expecting the intervention to do: how were changes in the behaviours of interest going to lead to better outcomes for users? As a result, I developed a model which illustrated our proposed mechanism of action.

The expert panel reviewed the list of suggested features from appendix 10 (Intervention planning doc) which led to the removal of 4: a diary for tracking medication use, a diary for tracking peak expiratory flow (PEF) rate, a tailored action plan, and a dedicated family & friends sections. The expert panel felt that evidence and personal experience suggested that use of diary tools was rarely sustained except by a few very motivated individuals. Instead regular prompts to think about current asthma symptoms based on the ‘Royal College Physicians 3 Questions’ (RCP 3Q) screening tool [162] was incorporated throughout the resource and in the automated emails. This asks the user about difficulty sleeping because of asthma, asthma symptoms during the day, and interference with usual activities. If users answer yes to even one question then further assessment of asthma control is indicated [163, 164].

Action plans work best when personalised to the individual [64] and the IT requirements of a truly tailored action plan was considered beyond the scope of this project. Instead a section was dedicated to promoting the use of action
plans, and encouraging individuals to visit their health professional to agree one if they did not have one. Rather than a dedicated family and friends section, the importance of positively involving family and friends was covered in general terms.

By the end of Phase 1, I had developed paper based versions of the proposed web pages ready for consideration by the expert panel and for use in think aloud studies. The pages were sent to all expert panel members for comment, usually to clinicians first then to the rest of the expert panel for comments.

5.3.2 Phase 2 results: Iterative refinement of the resource contents of the website

5.3.2.1 Think aloud studies and expert panel input

Eleven think aloud studies (see Table 5.3 for participant details) were conducted although one study (TA 08) was not completed as the website was not compatible with her type of computer which converted website text into braille (BrailleNote). Surprisingly only 4 of the 11 studies were undertaken in the participants’ own home, with most choosing to come to my place of work. Three of the participants (participants 3, 4 and 10) undertook 2 studies each. Each think aloud interview covered a slightly different range of topics as the resource was developed iteratively as demonstrated in Table 5.5.
Table 5.5 Topics covered per think aloud study

<table>
<thead>
<tr>
<th>Introduction</th>
<th>My asthma</th>
<th>Treatments</th>
<th>Asthma review</th>
<th>Exercise</th>
<th>Concerns</th>
<th>Queries</th>
<th>Stress Anxiety</th>
<th>Action plan</th>
<th>4 week challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td>TA01 †</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td></td>
</tr>
<tr>
<td>TA02</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td></td>
</tr>
<tr>
<td>TA03</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td></td>
</tr>
<tr>
<td>TA04 #</td>
<td>●</td>
<td>● (s2)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td></td>
</tr>
<tr>
<td>TA05 §</td>
<td>●</td>
<td>● (s3)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td></td>
</tr>
<tr>
<td>TA06</td>
<td>●</td>
<td>● (s2)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td></td>
</tr>
<tr>
<td>TA07</td>
<td>●</td>
<td>● (s2)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td></td>
</tr>
<tr>
<td>TA08 ‡</td>
<td>●</td>
<td>● (s3)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td></td>
</tr>
<tr>
<td>TA09 §</td>
<td>●</td>
<td>● (s3)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td></td>
</tr>
<tr>
<td>TA10 †</td>
<td>●</td>
<td>● (s3)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td></td>
</tr>
<tr>
<td>TA11 §</td>
<td>●</td>
<td>● (s2)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>○</td>
<td>●</td>
<td></td>
</tr>
</tbody>
</table>

†  TA01 and TA10 were same participant
#  TA04 and TA11 were same participant
§  TA05 and TA09 were same participant
‡  TA08 used a Braillenote computer, which was not compatible with our software so we were unable to complete the Think Aloud study.
¶  My asthma section eventually split into 3 sections (s1, s2, s3). With s1 being based mainly on the contents reviewed at the first 3 think alouds.

s1 – I have never been prescribed or used a preventer inhaler
s2 – I have a preventer inhaler but don’t really use it as prescribed
s3 – I have a preventer inhaler and mostly use it as prescribed
The thematic analysis of the think aloud transcripts identified 4 main themes: 1) ‘content’ – the actual words on the pages, and how relevant and understandable the information was; 2) ‘layout and navigation’ – the layout of pages or sections, and how easy it was to navigate around sections; and 3) ‘user experience’; and 4) graphics. The first 2 themes (contents and format) were further divided into 3 subsections each as shown in Figure 5.4. These 6 subsections were also noted as being positive, negative, or a suggestion for improvement. Graphics was a separate theme as personal communication from Lucy Yardley had advised that comments about appearance and graphics were often too specific to an individual’s tastes, and less useful in improving a websites acceptability or usability. With health behaviour change websites such as this, feedback on the message the page or section is trying to convey (e.g. the content) is the key area to focus on, along with the usability of the resource (layout and navigation).

Figure 5.4 Think aloud coding framework

Content
- Tone/Language
- Information provided
  - Clarity of Meaning

Layout and Navigation
- Section level
  - Page level

User experience

Graphics

Comments could apply to more than one code if appropriate. An example is a quote from a slide in an early think aloud study (Figure 5.5):
“And a wee fun fact kind of so, wow didn’t know that. Yeah I think that’s good to have that wee bubble because that’s it’s like, it’s scary enough to make you go oh actually this is really important but it’s not too scary that you are like oh my goodness I don’t even want to look at that so yeah that’s good.” (Participant 2, TA 03)

This whole quote was coded as ‘contents - information provided - positive’. However the second sentence was also coded under ‘contents - tone/language - positive’.

Using NVivo software, I generated quantitative data from the think aloud transcripts. Fifty one percent of the comments were positive, 15% negative and 34% containing suggestions for improvement. That almost half of comments were negative or suggestions for improvements implies that participants felt comfortable criticising the website in front of me, even though most knew I had developed it. Most comments related to the content of pages (78%), and the majority of these were positive (56%). In contrast, most comments about the website format (excluding graphics) were negative (69%) (Figure 5.6). This confirmed that the ground work done in Phase 1 around content had been successful, but that greater emphasis was needed on usability and presentation issues, as anticipated.
Content -making the website relevant and understandable

Participants were positive about the contents, and in particular the ‘level’ it was aimed at:

“It’s very clear in its intention, a website to help you stay healthy and manage your asthma better that’s exactly what level I’m at, I don’t have a detailed knowledge of what I’ve got or quite what I’ve got or quite how to look after it so it’s perfect for me.” (Participant 10, TA 01)

Users liked and identified with the key messages, for example that people with asthma should be ‘aiming for no symptoms’:
“I like a message of you know that’s what you should be aiming for, it might not be what you get right enough but at least you should be aiming for, or aiming for it the majority of the time, you know but you can if, you know going to have relapses, but I think that that’s really good because I don’t think many people actually say that to you to be honest.” (Participant 1, TA02)

“That’s good to know because again I just was putting up with it like if I was, if I wasn’t being able to breathe I would just be like oh I’m just having a bad day rather than being like ‘oh I should really be on the brown inhaler to stop this from happening’,” (Participant 3, TA04)

While there was universal agreement that quotes from patients and practice nurses were desirable within the website, there was some disagreement about how they should be presented:

“But I would give them maybe slightly more weight if they weren’t anonymous bizarrely. And it’s a real living patient that is living with asthma. And that kind of makes it more of a human.” (Participant 10, TA01)

In the following think aloud study this point was brought up by the interviewer:

“the quotes do you think, would you prefer to see something like female age 53 or is it not relevant? (researcher)

It’s not relevant to be honest because if I was twenty one and I was reading and they were fifty I would be thinking oh that doesn’t apply to me yet. The guy will be reading it and thinking oh that’s a woman thing.” (Participant 1, TA02)

Consequently, we kept quotes in the website but removed descriptions of who said them, as illustrated in Figure 5.7 below.
While patients on the whole agreed with the information provided, the one area where there was scepticism was in regard to how approachable participants’ practice nurses were:

“just trying to imagine sort of sitting down with my asthma nurse and saying I have a goal and this is what I want to achieve, I know what she’d say, she’d say I haven’t got time to discuss this! Let’s just stick to the tick boxes shall we?” (Participant 4, TA05)

**Layout and Navigation - making the website easy to use**

The majority of the comments regarding layout were page specific such as feeling that a given paragraph was too long. Where appropriate these were acted on immediately after the think aloud study in preparation for the next one. This was done by taking notes during the think aloud study using the unique page identifier along with the issue that was identified requiring action.

The importance of getting the home page right was clearly important to participants and generated much discussion.
“it doesn’t quite feel like a home page, that’s maybe not helpful. I’m trying to think what’s the best way to, it looks the same as every other page, I don’t know if you did something different to the header or something like that.” (Participant 4, TA05)

The home page therefore went through several iterations, summarised below in Figure 5.8.
Figure 5.8 Changes to home page during phase 2, from PowerPoint slide initially to final version

Early version
(PowerPoint)

Final version
(LifeGuide)
The second recurring theme in layout and navigation related to users ‘knowing where I am’.

“I say I might have said before maybe a little site map, you are on step 3 of 9, 4 of 9 and people know where they are going.” (Participant 4, TA09)

As a result I made it more obvious which section a user was in at a given time, and within the ‘4 week challenge section’ I changed it to visually show users progression as they made their way through this 4 stages of preparing to sign up to the ‘4 week challenge’.

**User experiences**

After completing the think aloud study users were asked how they might use the website in a real life setting and what would be barriers to its sustained use.

Users felt that they would have more confidence in such a resource if a health professional recommended it:

“I guess like in my annual review, if my nurse was like oh have a look at this. Like a wee leaflet or a wee business card or something like that and just was like have a look at that.” (Participant 2, TA03)

This finding is relevant for both future large scale RCTs, and the subsequent implementation and embedding of such a resource.

Several participants felt that it would be used to encourage recognition of symptom deterioration and timely visits to the GP:

“help people to be more aware of their good days and bad days, their triggers when they need to look at their self-medicating you know regimes, when to visit the GP because actually you realise it’s going down the slippery slope.” (Participant 1, TA02)

In particular this would be the case for people newly diagnosed:

“And I think people before you can start to manage a condition I think you need to know a lot about it you need to have the information don’t you and I think it provides a lot of interesting, useful information“ (Participant 6, TA07)

One potential barrier that was identified was if the content of the website was static, and not being updated, or new material being added:
“there is quite a lot but then you know after a while people have seen the website and then use drops off and I think it’s called the website winter so generally what happens most people go like that well I’ve done the website what more can I do” (Participant 4, TA05)

Table 5.6 explains the nature of the changes made during this phase as a result of input from the think aloud participants and the expert panel to each section.

Although not formally part of the ‘expert panel’, I shared the website with several other health professionals with an interest in asthma, mainly practice nurses, respiratory nurses and pharmacists. The main area of input by this group was providing a blank template action plan which users could print off, and sharing their own written self-management booklets with me, to ensure that the messages and information I was providing with the website was aligned with that from health professionals participants might see in local clinics.
<table>
<thead>
<tr>
<th>Section</th>
<th>Topics</th>
<th>Description of changes made</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Introduction pages† and Home page</td>
<td>Original one page introduction became 13+ page section. Both TA participants and expert panel highlighted that people with asthma are well known for underestimating their asthma severity, and suggested it was important I challenge this idea right at the start and illustrate to users how this resource could benefit them. First page presented user with questions designed to tease out limitations due to asthma. Then feedback provided for each question user ticked, along with tailored advice about which sections of the resource might benefit them most. Subsequent pages focused on identifying lifestyle goals relevant to users. Other changes included addition of a ‘landing’ page, combining links to sections to reduce the ‘buttons’ in the navigation bar from 11 down to 7, and rearranging the home page.</td>
</tr>
</tbody>
</table>
| 2       | My Asthma †       | Initially just one section, but became apparent that resource needed to be more tailored, and preventer therapy use was a good method of stratifying users, so users had to choose one of three options:  
            - I have never used/been prescribed a preventer  
            - I have been prescribed a preventer but don’t really use it  
            - I mostly/always take my preventer inhaler as prescribed  
            The think aloud study confirmed the contents of this section, with most changes focusing on improving readability, removing repetition and trying to achieve the right balance when explaining negative side effects versus potential benefits of inhaled steroids. |
| 3       | Treatments        | Layout of this section completely altered. It initially took the form of 6 pages users worked through with sideway steps for more information about different treatments. Section changed to have:  
            1. its own homepage (i.e. spoke and wheel layout) which allowed users to go directly to a treatment type without having to work through potentially irrelevant pages.  
            2. a visual representation of the asthma treatment ladder adapted from the BTS/Sign guidelines.  
            We were unable to meet requests to have pictures of individual inhalers. |
<p>| 4       | Asthma Reviews    | Focused on modifying the language used and simplifying messages. Altering layout of both individual pages and order of pages. Main message was to “aim for no symptoms” and this was very well received by users. Included a quiz covering what put people at risk of attacks – this was streamlined and made optional. |
| 5       | Action Plans      | Altered layout and clarity of wording, and quotes added to dilute the very factual nature of the information provided. Added a template of a blank action plan that users could print out and take to their health professional. |</p>
<table>
<thead>
<tr>
<th>Section</th>
<th>Topics</th>
<th>Description of changes made</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 (17 pages)</td>
<td>Physical Activity</td>
<td>Initially one generic section with the aim of promoting physical activity but was altered to become tailored to the individual’s activity status.</td>
</tr>
<tr>
<td>7 (18 pages)</td>
<td>Common concerns and queries</td>
<td>Originally had 8 concerns and queries, and a further 7 were added addressing topics originally not included as were felt to be covered elsewhere, or had seemed ‘too basic’. Reviewing this section served as a reminder that people quickly forget (or have never been told) even basic information about their asthma, and that having it here for those who need it was essential. Another major change was the wording of questions. One user commented that questions were just statements and did not make it clear than scenarios were amenable to change. So for example ‘I don’t exercise because of my asthma’ was changed to ‘I don’t exercise because of my asthma. Could I?’</td>
</tr>
<tr>
<td>8 (5 pages)</td>
<td>Stress &amp; Anxiety</td>
<td>Received mainly positive feedback. Links to online resources aimed at reducing stress and anxiety (e.g. online CBT) added.</td>
</tr>
<tr>
<td>9 (8 pages)</td>
<td>Take the 4 week Challenge</td>
<td>This section was specifically for users who had chosen option 1 or 2 during the ‘My Asthma’ section. Initially much confusion about the nature of the challenge with some users misunderstanding it completely. Thus pages were modified and more explanation added. Layout of pages were altered, in particular, to make it clear that there were 4 steps to work through, and it was made clearer how you were progressing through them (e.g colour strip across the top, which illustrated progress). One of the steps to the four week challenge was to anticipate barriers to taking preventer medication regularly and consider some solutions. Template barriers and solutions were provided, and these were added to by the think aloud participants.</td>
</tr>
<tr>
<td>10</td>
<td>Like to stop smoking?</td>
<td>This section was a link to an external site called ‘StopAdvisor’[165] and therefore not covered during the think aloud studies.</td>
</tr>
<tr>
<td>11 (1 page)</td>
<td>Useful info and links</td>
<td>Expanded during the think aloud to include more links to online mental health resources and information about the GP exercise referral scheme.</td>
</tr>
</tbody>
</table>

† Section 1 and 2 are core sections and all users are directed through them at first login, and can optionally visit again during future sessions.

# Refers to unique pages per section. Some pages are referred to in more than one section, but are only counted once here in the first section they appear.
5.3.2.2 NPT Analysis of Intervention Development

Throughout Phases 1 and 2 I had developed this intervention with reference to NPT, undertaking analysis of the intervention as outlined in Murray et al’s framework paper [111]. The final NPT analysis undertaken is shown below in Table 5.7.

Table 5.7 NPT analysis of intervention development

<table>
<thead>
<tr>
<th>Questions asked</th>
<th>Evaluation of Living Well with Asthma Development</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Coherence (i.e meaning and sense making by participants)</strong></td>
<td></td>
</tr>
<tr>
<td>Is the intervention easy to describe?</td>
<td>Yes.</td>
</tr>
<tr>
<td>Is it clearly distinct from other interventions?</td>
<td>Yes.</td>
</tr>
<tr>
<td>Do participants have a shared sense of its purpose?</td>
<td>FG suggest will have, but cannot be fully assessed until further evaluation where practice nurses are ‘recommending’ it.</td>
</tr>
<tr>
<td>What benefits will the intervention bring, and to whom?</td>
<td>Described within the ‘5 key tasks’ (section 5.2.3.1).</td>
</tr>
<tr>
<td>Are the benefits likely to be valued by potential participants?</td>
<td>Practices nurses – yes, Patients – persuading those with asthma of the benefits will be one of the biggest challenges as identified in section 5.2.3.1.</td>
</tr>
<tr>
<td>Will it fit with the overall goals and activity of the organisation?</td>
<td>Yes, promoting self-managing is considered a key strategy for managing increasing health service demands.</td>
</tr>
<tr>
<td><strong>2. Cognitive Participation (i.e commitment and engagement by participants)</strong></td>
<td></td>
</tr>
<tr>
<td>Are target users likely to think it is a good idea?</td>
<td>Yes, from FG and TA studies, both patients and nurses describe a gap in service provision this intervention should fill.</td>
</tr>
<tr>
<td>Will they see the point of the intervention easily</td>
<td>Yes, practice nurses seem frustrated that patients do not engage with asthma reviews, and adhere to medications. Patients feel they are not provided with information and practice nurses can be inaccessible.</td>
</tr>
<tr>
<td>Will they be prepared to invest time, energy and work in it?</td>
<td>Practices nurses – realistically within a consultation they have little capacity for additional work, therefore this has to overall lighten their workload. Patients – qualitative work suggests yes, but literature suggests in real life setting the answer is no. Therefore this requires as little work and time as is feasible.</td>
</tr>
<tr>
<td><strong>3. Collective Action (i.e the work participants do to make the intervention function)</strong></td>
<td></td>
</tr>
<tr>
<td>How will the intervention affect the work of user groups?</td>
<td>Living well with Asthma should be a website that practice nurses feel able to refer patients to during their asthma reviews, for example to provide further information advice, rather than used during the consultation. It could potentially reduce the pressure for practice nurses to cover everything in a review, as they can refer them to the website. It may reduce lack of patient satisfaction described during FG and TA with quality of asthma reviews.</td>
</tr>
<tr>
<td>Will it promote or impede their work?</td>
<td>As above, should promote.</td>
</tr>
<tr>
<td>Question</td>
<td>Answer</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>What effect will it have on the consultation?</td>
<td>Very little, as works to supplement the asthma review.</td>
</tr>
<tr>
<td>Will staff require extensive training before they can use it?</td>
<td>Living Well with Asthma was developed specifically so that it required no training.</td>
</tr>
<tr>
<td>How compatible is it with existing practices?</td>
<td>Entirely, as it is used entirely by patients in their own time at home.</td>
</tr>
<tr>
<td>What impact will it have on division of labour, resources, power, and responsibility between different professional groups?</td>
<td>It has been developed to supplement the asthma annual review, not replace it. However it will hopefully facilitate optimum self-management of their asthma by users, as an additional resource and will support patients wishing to taking more responsibility for their asthma management.</td>
</tr>
<tr>
<td>Will it fit with the overall goals and activity of the organisation?</td>
<td>Yes, we are promoting patients actively learning more about their own asthma and how they can manage it better.</td>
</tr>
</tbody>
</table>

**4. Reflexive monitoring (i.e. participants reflect on or appraise the intervention)**

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>How are users likely to perceive the intervention once it has been in use for a while?</td>
<td>One think aloud users queried the general static content that users will not go back unless new content is available. The entire site can be navigated in about 1 hour, therefore I anticipate that it may be used once or twice a year (perhaps prompted by the asthma review), or at times of increased disease burden such as during exacerbations.</td>
</tr>
<tr>
<td>is it likely to be perceived as advantageous for patients or staff?</td>
<td>All user group testing suggested it would be perceived positively by patients and practice nurses.</td>
</tr>
<tr>
<td>Will it be clear what effects the intervention has had?</td>
<td>Yes as ideally patients will attend more regularly for asthma reviews, experience fewer symptoms, better quality of life and take medications more optimally.</td>
</tr>
<tr>
<td>Can users/staff contribute feedback about the intervention once it is in use?</td>
<td>This should be possible.</td>
</tr>
<tr>
<td>Can the intervention be adapted or improved on the basis of experience?</td>
<td>Yes, one of the reasons for choosing LifeGuide software is how easy it is to modify interventions.</td>
</tr>
</tbody>
</table>

Undertaking this analysis informed some of the key decisions we made early on in the development such as deciding to make it independent of health professionals so they would not need training to use it for example, and encouraged me to ensure that it would not impede practice.

**5.3.2.3 Living Well with Asthma – final version ready for evaluation**

Completion of this phase resulted in the final website ready for evaluation in the RAISING trial [33]. Table 5.8 describes the final contents of the resource.
<table>
<thead>
<tr>
<th>Topic</th>
<th>Summary of content</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Introduction pages</strong> †</td>
<td>This section encourages users to recognise whether they are putting up with symptoms unnecessarily, and introduces concepts such as goal setting and its potential benefits.</td>
</tr>
<tr>
<td><strong>My Asthma</strong> †</td>
<td>There are three versions of this section tailored to current use of preventer therapy as chosen by the user.</td>
</tr>
<tr>
<td>1. I have never used/been prescribed a preventer</td>
<td></td>
</tr>
<tr>
<td>2. I have been prescribed a preventer but don’t really use it</td>
<td></td>
</tr>
<tr>
<td>3. I mostly/always take my preventer inhaler as prescribed</td>
<td></td>
</tr>
<tr>
<td>This section covers adherence and challenges negative beliefs about inhaled steroids.</td>
<td></td>
</tr>
<tr>
<td><strong>Treatments</strong></td>
<td>Provides information about different treatments. Links to videos to demonstrate inhaler technique and encourages users to consider whether they are on the correct ‘step’ of the asthma treatment ladder.</td>
</tr>
<tr>
<td><strong>Asthma Reviews</strong></td>
<td>Promotes attendance at asthma reviews outlining potential benefits to symptoms and quality of life. Prompts user to recognise if putting up with symptoms, and to recognise if they are at risk of asthma attacks.</td>
</tr>
<tr>
<td><strong>Action Plans</strong></td>
<td>Describes what action plans are and their potential benefits. Provides a template action plan that can also be used by practice nurses during asthma reviews in local health boards.</td>
</tr>
<tr>
<td><strong>Physical Activity</strong></td>
<td>Promotes benefits of physical activity, and challenges negative beliefs about exercising with asthma. Provides practical advice and tips to encourage users to increase their activity levels.</td>
</tr>
<tr>
<td><strong>Common concerns and queries</strong></td>
<td>Answers 15 common queries and concerns that people with asthma may have, developed from the literature, focus groups and during think aloud studies. For example: I am worried about taking inhaled steroids long term, should I be? Why are some days better than others?</td>
</tr>
<tr>
<td><strong>Stress &amp; Anxiety</strong></td>
<td>Promotes recognition of the role of stress on asthma, and how having asthma symptoms can lead to stress. Provides suggestions for reducing stress and anxiety.</td>
</tr>
<tr>
<td><strong>4 week Challenge</strong></td>
<td>The user is prompted to commit to taking their preventer inhaler regularly for 4 weeks. Users can choose from a list of provided ‘barriers’ to taking their inhalers and review suggested strategies or can free text their own. They may sign up to receive weekly emails during the challenge.</td>
</tr>
<tr>
<td><strong>Like to stop smoking?</strong></td>
<td>This links to an external website called ‘StopAdvisor’ [165]. This has been developed using LifeGuide software and further details are available elsewhere.</td>
</tr>
<tr>
<td><strong>Useful info/ links</strong></td>
<td>This re-lists information and useful links that have been included elsewhere in the website.</td>
</tr>
<tr>
<td><strong>Email reminders</strong></td>
<td>These emails are sent every two months. They all include the RCP 3 Questions to encourage the user to assess their current control and prompt them to visit the website or see their nurse or doctor if appropriate. There are also reminders to order inhalers, or other medications (e.g. in time for hay fever season), or if going on holidays.</td>
</tr>
</tbody>
</table>

† Section 1 and 2 are core sections and all users are directed through them at first login, and can optionally visit again during future sessions.
5.3.2.4 BCTs present in website

Assigning BCTs to the webpages generated much discussion between myself and SW. Areas of discussion centred mainly round whether a section went far enough to have BCT 1.2 (Problem solving) attributed. I had put pages providing video demonstration of inhaler use as BCT 6.1 (Demonstration of the behaviour) which upon discussion were changed to BCT 4.1 (Instruction on how to perform a behaviour). We debated the meaning of BCT 5.3 (Information about social and environmental consequences), as to whether it included consequences at a personal level e.g. work and social situations, or only at a more societal level. Ultimately, we agreed on the former.

In the end we agreed that 20 BCTs had been incorporated into Living well with Asthma website, covering 10 of the 16 behaviour change areas, and these are described fully in Table 5.9. The most commonly used BCTs were 5.1 (information about health consequences) and 6.1 (demonstration of the behaviour), followed by 1.2 (problem solving) and 4.1 (instruction on how to perform a behaviour).

Overall, in terms of BCT groupings I mainly used BCTs within ‘goals and planning’ as a key behavioural technique within the website (e.g. BCTs 1.1, 1.2, 1.3, 1.6 and 1.7) as seen in Table 5.9. This reflects my desire to ensure that we were not providing information on its own, but encouraging users to reflect on their own behaviour, and how they might work towards changing their behaviour to achieve better outcomes for themselves.

BCT groupings we did not cover at all were: Feedback and monitoring, reward and threat, regulation, identity, scheduled consequences, and covert learning. This reflects the limitations of a standalone digital intervention without integrated health professional support.
### Table 5.9 Behaviour change technique mapping of Living Well with Asthma website

<table>
<thead>
<tr>
<th>No/Label [107]</th>
<th>Definition</th>
<th>Sections</th>
<th>Example within LWWA website</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Goals and planning</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1 <strong>Goal setting</strong> (behaviour)</td>
<td>Set or agree on a goal defined in terms of the behaviour to be achieved</td>
<td>4 week challenge</td>
<td>Users commit to taking their preventer inhaler regularly for 4 weeks</td>
</tr>
<tr>
<td>1.2 <strong>Problem solving</strong></td>
<td>Analyse, or prompt the person to analyse, factors influencing the behaviour and generate or select strategies that include overcoming barriers and/or increasing facilitators (includes ‘Relapse Prevention’ and ‘Coping Planning’)</td>
<td>My asthma Concerns &amp; queries 4 week challenge</td>
<td>Users are prompted to consider reasons why they find it difficult to take their inhaler regularly (choosing from a list or free texting own). Users are then presented with sample strategies to overcome identified barriers.</td>
</tr>
<tr>
<td>1.3 <strong>Goal setting</strong> (outcome)</td>
<td>Set or agree on a goal defined in terms of a positive outcome of wanted behaviour</td>
<td>Intro</td>
<td>Users are asked to identify how their asthma can negatively affect their everyday lives. They are then asked to review positive outcome goals to overcome these negative effects</td>
</tr>
<tr>
<td>1.6 <strong>Discrepancy between current behaviour and goal</strong></td>
<td>Draw attention to discrepancies between a person’s current behaviour (in terms of the form, frequency, duration, or intensity of that behaviour) and the person’s previously set outcome goals, behavioural goals or action plans (goes beyond self-monitoring of behaviour)</td>
<td>Asthma Review</td>
<td>Asks validated questions to determine if currently putting up with asthma symptoms while believing themselves to be well controlled.</td>
</tr>
<tr>
<td>1.9 <strong>Commitment</strong></td>
<td>Ask the person to affirm or reaffirm statements indicating commitment to change the behaviour Note: if defined in terms of the behaviour to be achieved also code 1.1, Goal setting (behaviour) 4 week challenge</td>
<td></td>
<td>Users tick three statements confirming they are committed to taking their preventer inhaler regularly for the duration of the 4 week challenge.</td>
</tr>
<tr>
<td><strong>Social support</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.1 <strong>Social support</strong> (unspecified)</td>
<td>Advise on, arrange or provide social support (e.g. from friends, relatives, colleagues, ‘buddies’ or staff) or non-contingent praise or reward for performance of the behaviour. It includes encouragement and counselling, but only when it is directed at the behaviour</td>
<td>Concerns &amp; queries</td>
<td>‘Where can I talk to other people about asthma’ section details and links to online forum, local support groups, and advice lines.</td>
</tr>
</tbody>
</table>
| **Shaping knowledge** | **4.1 Instruction on how to perform a behaviour** | Advise or agree on how to perform the behaviour (includes 'Skills training') | Treatments  
Asthma Review  
Exercise  
Concerns & queries  
Action plans | Users are given step by step instructions on how to use an inhaler correctly. This is followed up by a video demonstration. |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>4.3 Re-attribution</strong></td>
<td>Elicit perceived causes of behaviour and suggest alternative explanations (e.g. external or internal and stable or unstable)</td>
<td></td>
<td></td>
<td>Describe common reasons why people with asthma put up with symptoms, illustrating that these beliefs are mistaken and providing alternative explanations for the symptoms.</td>
</tr>
</tbody>
</table>

| **Natural consequences** | **5.1 Information about health consequences** | Provide information (e.g. written, verbal, visual) about health consequences of performing the behaviour | Intro  
My asthma  
Treatments  
Asthma review  
Exercise  
Concerns & queries  
Action plans | Information provided that people who attend for regular asthma reviews have fewer symptoms and fewer asthma attacks. |
|--------------------------|-------------------------------------------------|-----------------------------------------------------------------|-------------------------------------------------|-----------------------------------------------------------------|
| **5.3 Information about social and environmental consequences** | Provide information (e.g. written, verbal, visual) about social and environmental consequences of performing the behaviour | Asthma review  
Exercise | | Information provided that people who attend for regular asthma reviews have fewer days off school and work, and fewer limitations in activities. |
| **5.6 Information about emotional consequences** | Provide information (e.g. written, verbal, visual) about emotional consequences of performing the behaviour | Concerns & queries | | People with asthma describe feeling embarrassed or ashamed taking inhalers in public. Information provided to overcome these concerns and increase confidence to use medications in public. |

| **Comparison of behaviour** | **6.1 Demonstration of the behaviour** | Provide an observable sample of the performance of the behaviour, directly in person or indirectly e.g. via film, pictures, for the person to aspire to or imitate (includes 'Modelling'). | My asthma  
Treatments  
Asthma review  
Exercise  
Action plans | Quotes for adults with asthma demonstrating how their lives changed for the better when they started taking their inhalers regularly. |
<table>
<thead>
<tr>
<th>Section</th>
<th>Description</th>
<th>Example Application</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>6.2 Social comparison</strong></td>
<td>Draw attention to others’ performance to allow comparison with the person’s own performance</td>
<td>My asthma Concerns &amp; queries In those who have identified that their asthma affects their work they are advised that this is the case with up to 40% of people with asthma.</td>
</tr>
<tr>
<td><strong>6.3 Information about others’ approval</strong></td>
<td>Provide information about what other people think about the behaviour. The information clarifies whether others will like, approve or disapprove of what the person is doing or will do</td>
<td>Asthma review Quote from practice nurse praising people who proactively attend for asthma reviews.</td>
</tr>
<tr>
<td><strong>Associations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>7.1 Prompts/cues</strong></td>
<td>Introduce or define environmental or social stimulus with the purpose of prompting or cueing the behaviour. The prompt or cue would normally occur at the time or place of performance</td>
<td>4 week challenge Emails Users who sign up to the 4 week challenge are sent weekly emails to remind them of the challenge and prompt them to continue.</td>
</tr>
<tr>
<td><strong>Repetition and substitution</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>8.2 Behaviour substitution</strong></td>
<td>Prompt substitution of the unwanted behaviour with a wanted or neutral behaviour</td>
<td>Exercise Users are provided with sample strategies to increase their levels of physical activity such as walking to the shops rather than taking the car, or giving up a TV programme for a dance class</td>
</tr>
<tr>
<td><strong>8.3 Habit formation</strong></td>
<td>Prompt rehearsal and repetition of the behaviour in the same context repeatedly so that the context elicits the behaviour</td>
<td>4 week challenge Strategies for prompting users to remember to take inhalers are suggested such as using them at the same time as teeth brushing or the evening meal.</td>
</tr>
<tr>
<td><strong>Comparison of outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>9.1 Credible source</strong></td>
<td>Present verbal or visual communication from a credible source in favour of or against the behaviour</td>
<td>Exercise Bradley Wiggins quote describing how asthma does not stop him exercising.</td>
</tr>
<tr>
<td><strong>Antecedents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>12.5 Adding objects to the environment</strong></td>
<td>Add objects to the environment in order to facilitate performance of the behaviour.</td>
<td>4 week challenge Strategies for prompting users to remember to take inhalers are suggested such having an extra inhaler at work, if they regularly forget their morning dose.</td>
</tr>
<tr>
<td><strong>Self-belief</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>15.1 Verbal persuasion about capability</strong></td>
<td>Tell the person that they can successfully perform the wanted behaviour, arguing against self-doubts and asserting that they can and will succeed</td>
<td>Exercise (external video) Users are directed to a video that promotes the message that anyone regardless of health status and fitness levels can successfully increase their levels of physical activity.</td>
</tr>
</tbody>
</table>
5.4 Discussion

5.4.1 Summary of findings

In this chapter I have demonstrated the feasibility of developing an evidence-based, theory guided, user friendly behaviour change intervention in the form of Living well with Asthma - a website to support self-management in adults with asthma. I have been guided by the MRC Framework on developing and evaluating complex interventions, and as a result directed much effort to the key, yet often overlooked, planning stages [100, 115]. I, with input from an expert panel, undertook recommended key tasks to guide content and methods [115] and through synthesis of empirical evidence, expert knowledge and experience, and incorporating theoretical concepts have co-designed with end users an evidence based behaviour change website for those with asthma.

Using the literature as a starting point I developed an understanding of barriers and facilitators to asthma self-management. Working through the 5 key tasks outlined by Campbell et al provided clear understanding of the problems and mechanisms for how the intervention could overcome these problems. This knowledge was successfully translated into the Living Well with Asthma intervention, utilising user experience at various stages. NPT analysis was undertaken to enhance the likelihood that what was developed was implementable in the longer term, should it prove to be effective. The BCT mapping exercise demonstrated that the resource incorporated multiple BCTs, a strategy which in some health domains has been associated with increased effect sizes [141]. In particular, I used goals and planning as a key behavioural technique within the website.

5.4.2 Strengths

This study followed recommended processes for developing complex evaluations, and was undertaken by a multidisciplinary team with a range of essential skills, knowledge and experience (including behaviour change theory and implementation theory). A key strength of this phase and the website I ultimately developed is in its co-design with potential end users, who had opportunity for input both at the early development planning stages in the form of focus groups, and also towards the end where their input via think aloud
studies was invaluable in improving the contents and usability of the resource. This ‘method’ has recently been the focus of a tutorial paper by members of the expert panel, and given a name: the ‘person based approach’ [166], providing rationale for incorporating multiple phases of qualitative work into the development of such interventions.

Using LifeGuide software allowed for a streamlined and iterative process of website development where I could undertake a think aloud study and then subsequently modify the website, or I could act quickly from feedback from the expert panel. Most computer programmers do not have a background in healthcare, and therefore removing the need to communicate user feedback about a health behaviour change website to a programmer made the process far more efficient.

Although within this PhD project as a whole, the focus was on developing and piloting the intervention, consideration of how this intervention might be implemented in the future was given consideration from the beginning. The consideration of the potential subsequent implementation of the website informed choices I made at these early stages in a number of ways. Firstly, I recognised the potential benefits of using an implementation theory (normalisation process theory) [101], choosing one I had experience of [148]. I found it most useful for designing the focus group topic guide, rather than the analysis, and for undertaking a NPT analysis during the development. Secondly, I spent time thinking about how such a website might work post trial i.e. in real life settings. This encouraged me to think about who would host the website and subsequently keep it up to date in the long term. This resulted in my choosing not to include forum/chat rooms, or include pictures of currently available inhalers. As a result I made links with Asthma UK and explored their possible role in long term management of the website. Thirdly, I also thought about what would prompt someone with asthma to visit this website - how would they find out about it? So, in addition to links with a high profile website such as Asthma UK’s I believed from my own personal experience as a general practitioner, that health professional recommendation would be important. This contributed to the decision to include practice nurses in the focus groups, recognising that practice nurses would need to ‘buy in’ to the idea of it, and promote it to patients if its use was going to be sustained long term. This was
found to also be very important to patients where most in the think aloud
studies felt they were most likely to visit a website like this if the practice nurse
advised them too. In addition, thinking about the long term plans I made links
with the NHS respiratory nurses and pharmacists who were members of the local
Managed Clinical Network for Respiratory conditions, to make them aware of the
project and arrange to discuss issues with them as required in an informal
manner.

5.4.3 Limitations

In the focus groups we included both practice nurses and adults with asthma,
which could be construed as a limitation. However there are advantages to
bringing together a diverse group of participants and we felt this was the case
here [167]. This can maximise the exploration of different perspectives, which
was pertinent here where differences in health professional and patient opinion
is a recognised barrier to optimal uptake of self-management practices [9].
However if time and resources allowed it may have been useful to have hosted
focus groups without nurses, as I may have got more information about what
patients felt was missing from an asthma review or what aspects were done less
well.

The adults with asthma participating in the focus groups and think aloud studies
had more severe asthma and were on more treatments than typical primary care
patients. This is because I only recruited 3 of the 10 participants from primary
care. I did not put an upper limit on asthma severity in my inclusion/exclusion
criteria which would have allowed me to focus in more on those with mild to
moderate asthma. I managed this situation by tempering the suggestions and
feedback from these end users with the practical experience of the practice
nurses present in the focus groups, and the respiratory physicians and GPs
(myself included) on the expert panel. If doing something similar again, I would
ideally aim for those participating in the co-design aspects to be more
representative of those who would ultimately be using the website. However, it
is clear from my reading that the important thing with usability testing is that it
is done in the first place, and it matters less who tests the website, so long as it
is tested [116]. This is in contrast with user testing to consider the actual
contents of the page and message the website is trying to convey, and ideally for that purpose the sample would be more typical of end users.

I undertook the think aloud studies, even though I was the person who had developed the website, and the participants knew this. Professor Lucy Yardley (expert panel) would ordinarily use independent researchers to undertake think aloud studies to avoid any risk that the user would feel unable to openly criticise the website. Therefore, I was concerned this could impact on the usefulness of the think aloud studies. In order to counter this I really emphasised that it was easy to make changes with the LifeGuide software and that critical comments were generally the most helpful. Exploring the scope of this limitation by counting negative comments was useful, as the high proportion of negative comments or suggestions for improvements indicates that participants did feel comfortable being critical of the website, and I did not get a sense that participants were holding back in any way. Overall the benefits outweighed this negative for me in this specific project as it allowed me to quickly and efficiently make changes to the resource without having to go through a third party.

5.4.4 Future considerations

The ultimate aim of following the updated MRC guidance on the development and evaluation of complex interventions is to reduce the number of interventions which are developed which are not sufficiently grounded in everyday experience to be translated into everyday use, and avoiding costly large RCTs which due to unforeseen circumstances are unable to answer the research question posed [100]. I believe the iterative methods of development used here should minimise this risk.

5.4.5 Conclusion

I have developed a resource which the results from the think aloud studies suggests is relevant and usable by its target audience. I have outlined the key steps which I went through, which included synthesis of knowledge and experience from our expert panel, exploring the literature, with overarching use of appropriate theory (behaviour change and implementation) and also with
input from potential stakeholders (adults with asthma and practice nurses) from an early planning stage. Such methods are rarely fully detailed in the literature, however I have published an abridged version of these methods to allow other researchers fully understand my processes [168]. In conclusion, this chapter demonstrates how data from a wide range of sources can directly and practically influence the contents of a self-management website. The next chapter details the evaluation of this resource.
Chapter 6: Evaluation of ‘Living Well with Asthma’: Randomised controlled trial of an Asthma Internet Self-Management Intervention (RAISIN study)

6.1 Overview & rationale

This chapter outlines the methods and results from the pilot, phase II, randomised controlled trial (RCT) of the Living Well with Asthma website, and discusses the findings in the context of the current literature. This evaluation study is referred to as the RAISIN study (Randomised controlled trial of an Asthma Internet Self-Management Intervention’)

A pilot study is ‘a version of the main study that is run in miniature to test whether the components of the main study can all work together’ [169], whereas a feasibility study is used to estimate important parameters that are needed to design the main study, such as ease of recruitment, standard deviations of outcome measures, and follow up rates [169, 170]. With this study I aimed to explore both feasibility and piloting. Both are essential to ensure that planned progression to a full scale, phase III RCT is appropriate in the first place, and then if warranted, can be undertaken with appropriate power to achieve definitive results.

6.1.1 Using NPT to inform trial design

As described in Chapter 3, NPT was used to facilitate this process, by informing the design of the trial with the aim of reducing issues with recruitment or data collection that so frequently impact of the usefulness of trial results, a process described as ‘optimisation of trial parameters’ [111]. Undertaking a NPT analysis as described here forces the trialist to understand the context where they are planning on undertaking their trial and investigating whether the trial procedures are compatible with existing practice. How will the trial affect the workload of those involved in the trial and those on the peripheries (health professionals, patients, support staff, admin). This framework provides a list of questions to consider when designing a trial. I used this framework iteratively when planning our trial design, and provide a written record of how it influenced the design here in Table 6.1.
Table 6.1 NPT analysis of RAISIN trial procedures

### Coherence (i.e meaning and sense making by participants)

<table>
<thead>
<tr>
<th>Question</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the trial easy to describe?</td>
<td>Yes</td>
</tr>
<tr>
<td>Is it clearly distinct from other studies?</td>
<td>Yes</td>
</tr>
<tr>
<td>Does it have a clear purpose for all relevant participants?</td>
<td>Practices can participate by either allowing researchers access to contact details of adults with asthma meeting inclusion criteria, and to send these potential participants an invite to the study. Alternatively practice nurses could hand out patient information leaflets to their patients during asthma reviews. The aim was to minimise workload to practices to optimise recruitment.</td>
</tr>
<tr>
<td>Do participants have a shared sense of its purpose?</td>
<td>There is little interaction if any between participants.</td>
</tr>
<tr>
<td>What benefits will the trial bring and to whom?</td>
<td>From a practice point of view participants may improve number of patients attending for asthma reviews and improved clinical outcomes for patients. For patients/participants themselves we hope participants may improve symptoms and quality of life.</td>
</tr>
<tr>
<td>Are these benefits likely to be valued by potential participants?</td>
<td>Practices are reluctant to take on any extra workload at present, even with financial recompense as many simply have no extra capacity for additional non patient workload. Adults with asthma often downplay their symptoms, so illustrating the potential benefits will be key to achieving recruitment targets.</td>
</tr>
<tr>
<td>Will it fit with the overall goals and activity of the organisation?</td>
<td>Overall aim is to promote optimum self-management, so yes.</td>
</tr>
</tbody>
</table>

### Cognitive Participation (i.e commitment and engagement by participants)

<table>
<thead>
<tr>
<th>Question</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are target user groups likely to think the trial is a good idea?</td>
<td>Practice staff describe people with asthma as reluctant to engage and may have doubts about the overall aim of the intervention itself. Patients themselves however are more positive about the provision of an extra resource for their condition, and understand that the trial is required for evaluation.</td>
</tr>
<tr>
<td>Will they see the point of the trial easily?</td>
<td>Health professionals should. Rationale for RCT covered in patient info leaflet</td>
</tr>
<tr>
<td>Will they be prepared to invest time, energy and work in it?</td>
<td>Primary care staff mostly will not be prepared to do this, therefore much effort has gone in to ensuring that recruitment has as little impact on practice workload as possible. Patient participants will have to give up approximately 2 hours of their time to participate, and given we provide no financial incentive we aim to be as accommodating as possible e.g. arranging trial visits during evenings and weekends and travelling to the participants homes.</td>
</tr>
</tbody>
</table>
Collective Action (i.e. the work participants do to make the intervention work)

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>How will trial procedures affect the work of user groups?</td>
<td>Practices will need to provide research staff with access to a practice computer for approximately one hour. If practices chose to give out patient information leaflets during reviews they will simply hand the leaflet to the patient and ask them to contact the research team if they are interested.</td>
</tr>
<tr>
<td>Will they promote or impede their work?</td>
<td>The trial should have no effect on their work.</td>
</tr>
<tr>
<td>What effect will it have on consultations?</td>
<td>Very little if any at all.</td>
</tr>
<tr>
<td>Will participation in the trial require extensive training for staff involved?</td>
<td>No.</td>
</tr>
<tr>
<td>How compatible is the trial with existing work practices?</td>
<td>Very compatible.</td>
</tr>
<tr>
<td>What impact will it have on division of labour, resources, power, and responsibility between different professional groups?</td>
<td>Nil</td>
</tr>
<tr>
<td>Will the trial fit with the overall goals and activity of the organisation?</td>
<td>There should be no impact.</td>
</tr>
</tbody>
</table>

Reflexive monitoring (i.e. participants reflect on or appraise the intervention)

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>How are users likely to perceive the trial once it’s been on-going for a while?</td>
<td>They may find that patients attend the practice prompted by the website.</td>
</tr>
<tr>
<td>Is it likely to be perceived as advantageous for patients or staff?</td>
<td>Practice staff may perceive it as advantageous if patients who previously didn’t attend for asthma reviews did attend.</td>
</tr>
<tr>
<td>Will it be clear what effects the study has had?</td>
<td>There may be little obvious impact at a practice level.</td>
</tr>
<tr>
<td>Can users/staff contribute feedback about study procedures?</td>
<td>Yes, participating practices will be provided with a summary of the results and offered opportunity to feedback. Intervention group participants are asked during follow up interviews about their experiences of participating in the study.</td>
</tr>
<tr>
<td>Can the study procedures be adapted/improved on the basis of experience?</td>
<td>This is a pilot study so this would be one of the main aims of the study.</td>
</tr>
</tbody>
</table>

This exercise was useful in this trial mainly to maximise the chances of us reaching our recruitment targets, by ensuring I had fully worked through the processes and the work that I was expecting mainly GP practices to undertake.

6.2 Aims & research questions

The aim of this evaluation was primarily to capture recruitment and retention data, but also to evaluate various outcome measures to allow for future sample size calculations, and to assess their suitability for inclusion in a future RCT.
I used the RE-AIM framework [113] to guide my methods, particularly in relation to choosing outcome measures. This framework has 5 domains: reach, efficacy, adoption, implementation and maintenance which ensures that an evaluation thinks beyond whether the intervention will work in a trial setting or not, to consider the broader picture of how it will perform in a real life setting. I considered each domain in turn and generated questions to answer or outcomes to measure which would provide evidence from this RAISIN evaluation for each of the domains. This is shown in Table 6.2.

<table>
<thead>
<tr>
<th>Domain</th>
<th>Description</th>
<th>Relevance to outcomes measured in RAISIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reach</td>
<td>An individual level measure of participation</td>
<td>Recruitment and retention rates. Characteristics of those eligible and ineligible.</td>
</tr>
</tbody>
</table>
| Efficacy   | Measuring both positive and negative outcomes, considering both clinical and behavioural outcome measures, and including quality of life, patient satisfaction/functioning perspectives. | Assessing feasibility of a range of outcome measures including:
Clinical: symptom scores/control, lung function, airway inflammation, health service contacts, medication use/changes' Behavioural: adherence, activation Patient centred measures: asthma specific and generic QOL measures. Patient experience questionnaire (PETS) |
| Adoption   | Refers to the proportion and representativeness of settings that may adopt a program. This dimension is organisational in nature, but there are individual considerations. | Out of those who were randomised to the intervention to what degree did they actually use the intervention? Do people who use the website differ to those who don’t? |
| Implementation | This refers to what extent the intervention is delivered as planned, and is practical enough to be effective in a representative setting. | What proportion of those allocated to the website used it, and how much? Understanding barriers to using the website – quantitatively using PETS and in depth interviews with those in the intervention arm.* Standalone internet delivered intervention means everyone offered same experience. |
| Maintenance | This refers to the extent interventions can become routine and embedded in every day practice. | PETS. Analysing website usability data. Qualitative interviews.* |

* separate project undertaken by colleague KS. PETS = problematic experiences of therapy scale, QOL = quality of life

This exercise led to me generating the research questions for the study.
6.2.1 Primary research questions

1. What are the likely recruitment and retention rates, over 12 weeks, for a trial comparing access to an internet asthma self-management resource (which aims to reduce symptom burden and improve quality of life in adults with asthma) with usual care, and how do those randomised differ from those screened and found to be ineligible?

2. For those in the intervention arm, how much is the website used, as determined by reviewing website usage statistics. Do those using the website differ from those who do not?

3. What are the changes, if any, in asthma control from baseline?

4. What are the changes, if any, in the asthma specific quality of life score from baseline?

6.2.2 Secondary research questions

1. What are the changes from baseline for the following clinical outcome measures:
   a. Lung function (via pre-bronchodilator spirometry)
   b. Fractional exhaled Nitric Oxide (FeNO)
   c. Health service contacts (scheduled and unscheduled)
   d. Asthma medication prescriptions/treatment levels?

2. What are the changes from baseline for the following behavioural measures:
   a. Self-reported adherence to medication
   b. Patient Activation Measure (PAM)

3. What are the changes from baseline for the following patient centred measures:
6.3 Methods

6.3.1 Ethical and management approval

The study received ethical approval from the West of Scotland Research Ethics Committee (REC) (reference WS/13/004) in March 2013. The study was reviewed initially at a panel meeting in January 2013, attended by me and supervisor Professor Mair. The REC was keen to discuss several issues. Firstly, one member questioned the validity of our approach at using a website to engender behaviour change, and expressed the view that they felt uncomfortable approving such a study without having a clearer idea of the contents of the website. This was resolved by discussion and agreement that I would submit screenshots of the website to the committee for review prior to approval. NHS Greater Glasgow and Clyde Research and Development (R&D) agreed to sponsor the study.

The other main concerns were regarding recruitment methods. Firstly they queried my method of screening out unsuitable patients at GP practice level. As once a search for potential participants was completed, the GPs would look at the list to screen out unsuitable patients such as those with palliative illness or cognitive impairment. One committee member questioned the reliability of this method feeling that the computer would be more reliable than the GPs looking at the list. It was explained that one of the main barriers to achieving focussed GP searches was the variability in coding between practices particularly in terms not featured in the Quality and Outcomes Framework (QOF), and it was agreed at the meeting that our approach was appropriate. Following this meeting, the initial correspondence from the REC highlighted a further issue which had not been raised at the meeting itself: they stipulated that patients were not to be
contacted a second time if they did not respond to our initial mailing. I responded in writing by explaining our previous experiences of exceptionally difficult recruitment to asthma studies. The REC agreed that, if required to achieve recruitment targets, I could follow up an initial mailing with either a telephone call or a second letter, provided the reply slip was modified to make explicit that it would be possible that the research team could contact them a second time. As a result the following line was added: “We may contact those who don’t respond to the initial mailing one further time either by telephone or by post.” as illustrated in the reply slip. All correspondence to and from the REC is found in appendix 11.

6.3.2 Recruitment

6.3.2.1 Mailings from primary care

Twenty primary care practices agreed to help with this research. This involved allowing either me, a colleague (KS), or a member of the Scottish Primary Care Research Network (SPCRN) to visit the practice and undertake a search for patients with a diagnosis of asthma aged 16 years or over. Due to high numbers of asymptomatic patients being identified the search strategy was refined over the recruitment period, to try and target our mailings more towards participants with active asthma who were requesting reliever therapy within a recent timescale.

Patients identified through the search, and approved by the practice, received a letter (appendix 12) on their own GP headed note paper inviting them to indicate their interest in the study. The mailing pack included a reply slip, a reply paid envelope, and a patient information leaflet (appendix 12). Potential participants indicated their interest in the study by replying with their contact details directly to me, via mail, email or telephone.

As discussed in section 6.3.1 we had ethical approval to follow-up an initial mailing with either a telephone call or a second mailing. Patients were to be called no more than once and informed that we were still recruiting and asked if they were interested in hearing more about the study. The second mailing was the same as the first.
Based on experience from previous asthma studies [171-173], I projected a 10% positive response rate, of which 25% would translate into randomisations. Therefore to randomise 50 we would need to screen 200, and therefore invite 2000.

6.3.2.2 Other recruitment strategies

Posters (see appendix 13) were put up locally in pharmacies and in the university. I had ethical approval to approach patients who had previously participated in asthma studies, and patients attending the difficult asthma clinic at Gartnavel General Hospital. I also had ethical approval to recruit via snowballing - a method where those in the study can recommend it to friends or family.

6.3.3 Screening for eligibility

Once a positive response was received, potential participants were screened over the telephone. This involved checking for obvious exclusion criteria, verbally assessing their symptoms using the asthma control questionnaire (6 question version), and finally ensuring they met the rest of the inclusion criteria. Once confirmed that they met eligibility criteria a date for a baseline visit was arranged. Potential participants were advised that they should contact us if their asthma flared up between screening telephone call and baseline visit, and that on the day of the visit inhalers should be withheld to allow for pre-bronchodilator spirometry to be undertaken. This telephone screening process was standardised by developing a checklist, a copy of which can be found in appendix 14.

6.3.4 Inclusion criteria

As outlined in the previous chapter, our development planning exercise had shown that adults with uncontrolled asthma were most likely to benefit from this intervention. An Asthma Control Questionnaire (ACQ) ≥ 1 has been shown to be an acceptable cut off for established poor control so we only included adults above this cut off [155]. Participants needed to have symptoms for at least a year, to increase the likelihood we were including individuals with genuine
asthma, rather than viral related wheezing episodes. The inclusion criteria were:

1. Written informed consent
2. Age 16 years or older
3. Diagnosis of asthma by a health professional, and duration of asthma symptoms > 1 year
4. ACQ (6 questions version) ≥ 1 suggesting poorly controlled asthma
5. Ability to access the internet via desktop or laptop (tablets and smartphones not sufficient)

### 6.3.5 Exclusion criteria

This intervention was designed to be used by individuals with mild to moderate asthma. Given there was no monitoring of individuals between study visits we had to minimise the risk to patients, therefore we excluded people with unstable or severe asthma. Our exclusion criteria were:

1. Unstable asthma as defined as the presence of 1 or more of the following events in the 4 weeks prior to randomisation:
   a. asthma related hospital admission,
   b. A&E attendance for asthma
   c. ‘out of hours’ visit of patients to the GP for asthma
   d. GP visit to patient at home for asthma
2. frequent asthma exacerbations with > 4 courses of oral prednisolone in the 12 months prior to randomisation
3. Presence of active lung disease other than asthma
4. Mental impairment or language difficulties that make informed consent impossible
5. Terminal illness
6. Cognitive impairment

### 6.3.6 Study design

The study was a 12 week\(^1\) parallel group randomised controlled trial. Blinding of the participants was not possible due to the nature of the intervention. Blinding

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\(^1\) Follow up visit was at 12 weeks, or as soon as possible after this date
of myself as researcher was not possible as I was involved in all stages from recruitment, randomisation, follow up and data analysis. Potential sources of bias were minimised where possible for example by collecting baseline data prior to randomisation, and ensuring concealment by using an automated interactive voice response system (IVRS) for group allocation. The data collected was managed independently by an experienced clinical trials unit (CTU) at the Robertson Centre for Biostatistics (RCB), University of Glasgow.

I was fortunate that alongside this project my colleague KS was able to undertake qualitative interviews with those in the intervention group, although they do not feature as part of this project itself.

6.3.7 Trial management

6.3.7.1 Routine trial management

The routine management of the trial was coordinated by the Trial Management Group (TMG). This comprised of me and all four PHD supervisors. The TMG monitored the progress of the trial ensuring that the protocol was adhered to and met bimonthly, with monthly recruitment reports via email.

6.3.7.2 Delegation log

I was chief investigator (CI) and led this evaluation. I coordinated recruitment, with support from SPCRN and Dr K Saunderson (KS). Screening assessment, baseline visits and follow-up visits were completed me or KS. RCB handled anonymised trial data. I undertook the statistical analysis of trial data, with support from statisticians at RCB.

6.3.7.3 Protocol amendments

Any changes to the study protocol were made following agreement with the TMG, and subject to approval from R&D and REC where required.

6.3.7.4 Criteria for discontinuation

The study planned to end when the TMG agreed that either:
- The planned sample size has been achieved.
- The recruitment is so poor that completion of the trial is not feasible.

6.3.7.5 Adverse events

Adverse events (AEs) are defined as an adverse change in health that occurs while a patient is taking part in a study. I planned to record only AEs which were outcome measures.

6.3.7.6 Serious adverse events

A serious adverse event (SAE) is any adverse event, which results in:

1. Death,
2. Is life-threatening,
3. Inpatient hospitalisation or prolongation of inpatient hospitalisation,
4. Persistent or significant disability/incapacity that interferes with the person’s ability to conduct normal activities of daily living,
5. Congenital anomaly or birth defect.

The term life-threatening’ in the definition of ‘serious’ refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if it were more severe. Hospitalisation for a pre-existing condition, including elective procedures, which has not worsened, does not constitute a serious adverse event. An important medical event may be considered a SAE when, based on appropriate medical judgment, it may jeopardise the subject and/or may require medical or surgical intervention to prevent one of the outcomes listed.

Any SAE that was ongoing on completion of the trial was to be followed until it resolved or stabilised, returned to baseline or could be attributed to factors unrelated to the study.

Serious adverse reactions (SARs) and suspected unexpected serious adverse reactions (SUSARs) were not applicable in this study as this was not a clinical trial of an investigational medicinal product (CTIMP).
6.3.7.7 Reporting of serious adverse events

The plan was for KS or I to record SAEs at follow-up. All SAEs were assessed for seriousness, causality, expectedness and severity. This assessment was the responsibility of the chief investigator (CI), which was me, or Prof F Mair during my maternity leave. Any SAEs were sent to the sponsor and REC in an annual safety report. Detailed records of all SAEs were held in the trial master file.

6.3.8 Baseline characteristics

Describing baseline characteristics is important to illustrate that both groups are roughly equal, which should be the case if robust randomisation procedures are followed. Anecdotally there is concern that only fit, healthy adults put themselves forward for this type of study, therefore it is helpful to show that this sample have co-morbidities and in this way are representative of the wider population. Co-morbidity counts were calculated by agreeing with FM and SW a list of what conditions counted as a condition and totalling them up. This list was based on medical problems listed in the case report form (CRF) alongside the free text medical conditions. No weighting was given to particular conditions, and they are listed in appendix 15.

All baseline characteristics are presented descriptively.

6.3.9 Primary outcome measures

6.3.9.1 Recruitment and retention

I recorded the number of invites sent, number of positive responses received, proportion who did not meet criteria, and ultimately numbers randomised. Retention refers to those who were available for follow-up visit, and therefore completed the study (including those who didn’t actually use the website).

6.3.9.2 Website usage

I measured use of the website in a number of ways

1. Number of eligible users who log in
2. Number of times users log in
3. Length of time users spend on website
5. Users responses to questions about impact of asthma on their lives
6. Choice of tailored sections:
   a. I have never been prescribed a preventer inhaler
   b. I have been prescribed an inhaler but don’t really use it
   c. I have a preventer and usually use it as prescribed

I have also compared users of the website versus non-users using age, gender, SIMD and baseline measures of asthma control (ACQ), quality of life (mini-AQLQ) and adherence markers (MMAS, and % percentage prescribed ICS taken). I define a non-user as someone who didn’t log in at all, or used the website for <10 minutes. Ten minutes was chosen as this is the approximate time taken to complete the core modules. This data is important to try and understand how the intervention works or doesn’t work in practice, and inform any changes that may be beneficial before further evaluation.

6.3.9.3 Asthma Control Questionnaire (ACQ) score

The ACQ is widely used by both researchers in clinical trials and clinicians in the routine management of patients, and was the symptoms control outcome of choice for this study. The alternative would have been the Asthma Control Test, which has similar sensitivity and specificity for detecting poorly controlled asthma [174, 175], and is also recommended as a core asthma outcome [135]. Overall, I chose the ACQ, due to being familiar with it, and cost, as the ACQ was free to me as a PhD student.

The ACQ is a 7 item scoring system (6 questions filled in by participants and one lung function measure filled in by a health professional) [158]. The final score is the mean of the 7 responses (0 = good control, 6 = poor control). In both settings the absolute score is meaningful i.e. ACQ ≥ 1 implies poorly controlled asthma [155], and the minimally important difference (MID) is recognised to be a change in score of ≥0.5 [176]. The MID is defined as:
‘the smallest difference or change in score which clinicians perceive as beneficial and would mandate, in the absence of troublesome side-effects and excessive cost, a change in the patient’s management’ [176]

As a result the ACQ has been used as one of two clinical primary outcomes in this pilot study as it would be a likely candidate for any future full scale RCT evaluating this intervention. I report both the change in scores, and the proportion whose change in score meets the MID. I also report the proportion of participants who would be classed as controlled by follow up (i.e. ACQ <1).

6.3.9.4 Mini Asthma Quality of Life Questionnaire (AQLQ) score

This was the obvious choice for me for outcome for measuring asthma specific QOL, as it is commonly used asthma specific measure [8]. The mini-AQLQ is a 15 item self-administered questionnaire developed from an original 32 item AQLQ [177], and is recommended as a supplemental outcome for asthma evaluations [135]. It has 4 domains: symptoms (5 items), activity limitation (4 items), emotional function (3 items) and environmental stimuli (3 items). As with the ACQ the MID for the mini-AQLQ is a change in score of ≥ 0.5. One potential issue with this mini-AQLQ is item 7 which asks ‘How much of the time during the last 2 weeks did you feel bothered by or have to avoid cigarette smoke in the environment?’ Since March 2006 smoking in public places has been banned in Scotland, and in all countries in the UK by July 2007, which renders this question potentially less relevant than previously.

6.3.10 Secondary outcome measures

6.3.10.1 EQ-5D

The EQ-5D [178, 179] is a generic measure of health developed by the Euroqol Group (www.euroqol.org). I chose to include the EQ-5D as it is a frequently used generic measure of health related quality of life. It is the preferred method for the UK National Institute for Health and Care Excellence (NICE), particularly when attempting to calculate quality adjusted life years (QALYs). While cost-effectiveness is not an outcome measured in this study, it will be in future studies, and therefore piloting of this outcome was indicated.
The EQ-5D has two parts, both designed to be completed by the participant. The first defines health in terms of 5 dimensions: mobility, looking after myself, doing usual activities, having pain or discomfort and feeling worried, sad or unhappy. Each dimension is broken down into 3 categories covering whether the individual has no problem, some problems, or a lot of problems within the given dimension. These dimensions are found on the first page of the questionnaire, and potentially 243 health states can be defined by this instrument. Each of these 243 health states can converted into a single health utility score, by applying a European valuation set to the scores. Health utility scores are anchored by 0 (dead) and 1 (perfect health).

The second part of this health measure captures a self-rating of health status (‘How good is your health today’) on a visual analogue scale (VAS) ranging from 0 (the worst health you can imagine) and 100 (the best health you can imagine).

A copy of the questionnaire can be found within appendix 16.

There is no defined minimally important difference (MID) for the EQ-5D specific to asthma populations. However, one study looking at a range of datasets (included chronic obstructive pulmonary disease but not asthma) suggests that MID for the health utility score is 0.074 [180]. This is similar to a study concentrating on cancer patients which estimated the MID for UK populations of 0.08 for the health utility scores and 7 for changes in the VAS [181]. How these figures relate to a UK sample of adults with mild to moderate asthma is not clear.

There is rationale from COPD studies for using both generic (e.g. EQ-5D) and disease specific measures of health related QOL (e.g. AQLQ) in this case in order to capture the full effects of illness on an individual [182], justifying the use of two QOL measures.

6.3.10.2 Morisky Medication Adherence Scale (MMAS)

The Morisky Medication Adherence Scale (MMAS) is an 8 item generic medication adherence scale [183]. I chose this measure because it can be easily adapted to cover inhalers (many questionnaires talk only about pills), it is quick and easy to
use and interpret. Although self-report has its limitations, it can be useful and accurate, particularly where participants feel they can be honest about their answers [60]. To this end, I made it clear at the start of the trial visits that this information was not reported back to GPs, and that being realistic about their inhaler use was most helpful to the study. With the MMAS the results were also categorised as high adherence (score of 6 to 8) or low adherence (score of < 6), along with overall scores. The MID for the MMAS is reported as a change in score ≥2 [184].

### 6.3.10.3 Patient Activation Measure (PAM)

The PAM is a 13 item questionnaire which gauges to what degree an individual has the knowledge, skills and confidence to manage their own health and healthcare. Answering the 13 questions provides a ‘raw’ score which is then converted into the ‘activation’ score. This activation score is used in two ways - firstly to determine if there has been a change in the overall activation score, and secondly it allows users to be stratified into one of 4 progressively higher activation levels (Table 6.3). Ideally an intervention such as Living Well with Asthma should help an individual move up a level towards the stage of maintaining a desired behaviour, therefore the proportion of individuals moving up a level is also reported as well as the change in the activation score itself.

<table>
<thead>
<tr>
<th>Level</th>
<th>Activation Score</th>
<th>Summary</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0 - 47.0</td>
<td>Disengaged and overwhelmed</td>
<td>Individuals are passive and lack confidence. Knowledge is low, goal-orientation is weak, and adherence is poor.</td>
</tr>
<tr>
<td>2</td>
<td>47.1 – 55.1</td>
<td>Becoming aware but still struggling</td>
<td>Individuals have some knowledge, but large gaps remain. They believe health is largely out of their control, but can set simple goals.</td>
</tr>
<tr>
<td>3</td>
<td>55.2 – 67.0</td>
<td>Taking action</td>
<td>Individuals have key facts and are building self-management skills. They strive for best practice behaviours, and are goal orientated.</td>
</tr>
<tr>
<td>4</td>
<td>&gt; 67</td>
<td>Maintaining behaviours and pushing further</td>
<td>Individuals have adopted new behaviours, but may struggle in times of stress or change. Maintaining a healthy lifestyle is a key focus.</td>
</tr>
</tbody>
</table>

An alternative questionnaire we could have used instead of the PAM was the Knowledge, Attitudes and Self-Efficacy Asthma Questionnaire (KASE-AQ) which
up until more recently has been widely used and is asthma specific [185]. Each domain (knowledge, attitudes and self-efficacy) has 20 questions each. It is now generally accepted that the knowledge domain is outdated and no longer fit for purpose, with recent studies using only the attitudes and self-efficacy questions [186]. Overall, I felt that the 13 item PAM best matched what we were hoping this intervention would achieve and chose it over the modified KASE-AQ, with the added benefit of minimising questionnaire workload for participants.

6.3.10.4 Lung function via spirometry

Spirometry measures how an individual exhales volumes of air as a function of time, and I aimed to measure pre-bronchodilator spirometry, which is considered a ‘core asthma outcome’ for asthma treatment evaluations [135].

I used a Vitalograph Micro MO5523 portable device, and aimed to measured pre-bronchodilator spirometry. I received training from the manufacturer. In accordance with the ATS/ERS statement and manufacturers guidance, a calibration check was undertaken daily. The best of 3 measures were recorded (automatically by the device), and the device presented the ‘best’ version.

Spirometry testing measures two main volumes: the forced vital capacity (FVC) and the forced expiratory volume in 1 second (FEV\textsubscript{1}). The FVC is the volume of air delivered during a complete and forceful expiration, from full inspiration. The FEV\textsubscript{1} is the volume expired in the first second of the FVC measurement. Two further measures can be derived from these two. Firstly the ratio of FEV\textsubscript{1} to FVC (FEV\textsubscript{1}/FVC), which is mainly used to define airflow obstruction, with values less than 70% being suggestive of airway limitation such as that seen in asthma [187]. The second is the FEV\textsubscript{1} % of predicted, where the predicted value is calculated from age, gender, height and weight, which are inputted to the device before testing.

The Vitalograph also measured peak expiratory flow (PEF). Single results are of less use as a lung function measure, although serial measurements can be useful. Spirometry and PEF are considered core pulmonary physiology outcomes for describing asthma populations and assessing the response to an intervention in
clinical trials [188]. In particular, FEV\textsubscript{1} and PEF are commonly used as outcome measures in asthma studies [6].

In this study I report FEV\textsubscript{1}, FEV\textsubscript{1} % of predicted, FVC, FEV\textsubscript{1}/FVC, and PEF. The ATS/ERS provide guidance about what is considered an acceptable spirometry test [189]. In particular they state that, after three acceptable spirograms have been obtained, the two largest values of FVC must be within 0.150 L of each other, and the two largest values of FEV\textsubscript{1} must be within 0.150 L of each other. If these criteria are not met then continue testing until acceptability is reached, 8 tests have been performed, or the patient can no longer continue. The other important stipulation is that certain bronchodilators should not be taken within a defined time period of the test occurring, for example no short acting bronchodilators within 4 hours.

6.3.10.5 Lung inflammation: Fractional exhaled nitric oxide (FeNO)

FeNO is an inflammatory biomarker, and provides information on airway inflammation, and is now an established measure for monitoring asthma (and adherence to ICS), particularly in trials and in secondary care [4, 135]. It is measured in parts per billion (ppb). I used a NIOX MINI® Airway Inflammation Monitor to measure the FeNO. ATS/ESR guidance [190] suggests a minimum of 2 measurements per individual; however, NIOX MINI® manufacturer recommends only one. Given this was a pilot study I undertook a single measure only.

FeNO levels are high in those with uncontrolled asthma, and reduced following steroid therapy [191]. The normal range for adults varies. The ATS/ERS guidance defines the normal range as between 5 ppb and 35 ppb, whereas the NIOX MINI® manufacturer recommend stratifying adults as either low (<25 ppb), medium (25-50 ppb), or high (>50 ppb). The clinical guide to interpreting FeNO values provided by the NIOX MINI® manufacturer advises that scores < 25 suggest either that the patient is adherent to adequate inhaled corticosteroids (ICS), or that another diagnosis should be considered. Scores > 50 are consistent with inadequate ICS treatment, for example as the dose is too low, adherence is suboptimal, or inhaler technique is poor. This outcome is expensive, each single use mouthpiece costing approximately £7, however the manufacturer of the NIOX MINI® Aerocrine Ltd provided the device and mouthpieces.
6.3.10.6 Changes to regular asthma medications

This outcome is described in 4 ways:

1. Change in number of puffs of reliever medication used in an average week.
2. Percentage of prescribed ICS actually taken in an average week.
3. Equivalent beclometasone dose (mcg) prescribed at baseline and follow up.
4. Change in step of the British Thoracic Society (BTS) treatment ladder (range 1-5).

The ideal situation is for patients to be on adequate ICS that controls their symptoms so that reliever inhaler use is minimised, and ideally less than 4 puffs a week. Consequently stepping up the BTS treatment ladder is not necessarily a sign of deteriorating asthma, but could be a sign that a patient has moved onto the correct treatment to manage their symptoms better.

6.3.10.7 Oral prednisolone use and health service contacts.

Courses of oral prednisolone are a marker of severe asthma exacerbations [34]. A second course prescribed within 7 days of the first finishing was counted as a single course, as outlined by the ATS (American Thoracic Society taskforce [34]. We also recorded whether the participants had any contact with health services for their asthma over the study period, including routine asthma reviews, non-routine asthma appointments or unscheduled hospital or emergency room visits.

6.3.10.8 Problematic experiences of therapy scale (PETS)

This questionnaire was only for individuals in the intervention arm. It measures difficulties experienced in relation to following the advice provided by an intervention [192]. It has 4 ‘domains’ which cover 1) whether symptoms themselves impede ability to follow advice, or are worsened by the advice, 2) uncertainty about how to follow the advice, 3) doubts about the efficacy of the website advice and 4) practical obstacles to following the advice such as time or opportunity. It was the only patient experience questionnaire available which was suitable for this type of standalone non-pharmacological intervention, as
most experience questionnaires focused on experience of face to face consultations [193] or inpatient stays [194] or about pharmacological treatments [195, 196].

6.3.11 Statistical analysis

Analysis was conducted on an intention to treat basis on randomised individuals. Continuous data were summarised as mean and standard deviation (SD) or range, or as median and inter-quartile range (IQR). Categorical data was presented as counts and percentages. Linear regression was used to estimate differences in continuous outcomes between groups at follow up, adjusting for baseline scores. Estimated between-group differences are reported with a 95% confidence interval (CI) and p-value. For continuous outcomes that were not normally distributed, changes from baseline were compared between groups using Wilcoxon Rank Sum Tests. Categorical variables were compared between groups using Fisher’s exact test. All analyses were carried out using SPSS Statistics 22 and Microsoft Office Excel.
6.4 Results: Baseline characteristics of participants

This section details the baseline demographics, medical history, asthma history, asthma medications and contacts with health services for the participants as a whole (n =51, all those who completed a baseline visit) and per group. These results confirm the groups were evenly matched, as expected in view of the robust randomisation procedures used.

6.4.1 Baseline demographic characteristics

The baseline demographic characteristics are shown in Table 6.4. The average age of participants was just over 45 years, and the majority were female which is consistent with evidence that asthma is more prevalent in women [2], although contrasts with participant rates in studies published to date 54% of the participants in the RCTs included in the metareview were male [8]. The proportion of smokers in this study is lower than you would expect to find in the general asthma population, despite the spread across deprivation quintiles being reasonably even. The majority of participants were employed and had completed some form of further education beyond high school at 65%, which is just higher than the Scottish school leavers rates of 54.7% in 2013 [197]. However, this data only includes those attending further education before the age of 30 years age.
Table 6.4 Baseline demographic characteristics of study population per group, data are n(%) unless otherwise stated

<table>
<thead>
<tr>
<th></th>
<th>Overall (n = 51)</th>
<th>Comparison (n = 26)</th>
<th>Intervention (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) mean(SD)</td>
<td>45.5 (15)</td>
<td>46.4 (14)</td>
<td>44.6 (17)</td>
</tr>
<tr>
<td>Female</td>
<td>38 (75)</td>
<td>20 (77)</td>
<td>18 (72)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>48 (94)</td>
<td>24 (92)</td>
<td>24 (96)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (6)</td>
<td>2 (8)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Smoking status:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>5 (10)</td>
<td>2 (8)</td>
<td>3 (12)</td>
</tr>
<tr>
<td>Former smoker</td>
<td>18 (35)</td>
<td>11 (42)</td>
<td>7 (28)</td>
</tr>
<tr>
<td>Never smoked</td>
<td>28 (55)</td>
<td>13 (50)</td>
<td>15 (60)</td>
</tr>
<tr>
<td>SIMD quintile (1 = most deprived, 5 = least deprived):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIMD 1</td>
<td>14 (28)</td>
<td>7 (27)</td>
<td>7 (28)</td>
</tr>
<tr>
<td>SIMD 2</td>
<td>11 (22)</td>
<td>6 (23)</td>
<td>5 (20)</td>
</tr>
<tr>
<td>SIMD 3</td>
<td>9 (18)</td>
<td>4 (15)</td>
<td>5 (20)</td>
</tr>
<tr>
<td>SIMD 4</td>
<td>5 (10)</td>
<td>3 (12)</td>
<td>2 (8)</td>
</tr>
<tr>
<td>SIMD 5</td>
<td>12 (24)</td>
<td>6 (23)</td>
<td>6 (24)</td>
</tr>
<tr>
<td>Employment status:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>25 (49)</td>
<td>11 (42)</td>
<td>14 (56)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>8 (16)</td>
<td>3 (12)</td>
<td>5 (20)</td>
</tr>
<tr>
<td>Retired</td>
<td>9 (18)</td>
<td>5 (19)</td>
<td>4 (16)</td>
</tr>
<tr>
<td>Student</td>
<td>2 (4)</td>
<td>1 (4)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Other</td>
<td>7 (14)</td>
<td>6 (23)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Education level:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary education</td>
<td>18 (35)</td>
<td>7 (27)</td>
<td>11 (44)</td>
</tr>
<tr>
<td>Tertiary/further education</td>
<td>33 (65)</td>
<td>19 (73)</td>
<td>14 (56)</td>
</tr>
</tbody>
</table>

SIMD = Scottish Index of Multiple Deprivation

6.4.2 Baseline medical history

Table 6.5 shows the baseline medical history for the participants as a whole, and each individual group. This demonstrates that the intervention group and comparison groups were well matched in terms of their body mass index (BMI) and medical conditions.
The number of co-morbidities is shown in Table 6.6. As expected given the age group included in this study only 2 participants had asthma on its own, with all other participants having at least 1 co-morbidity.

### 6.4.3 Baseline asthma history and medications

Table 6.7 describes the asthma history for the 51 participants who completed the baseline visit. This demonstrates that those in the study had asthma for a considerable length of time, and the majority were on step 2 or 3 of the asthma treatment ladder indicating they were already prescribed ICS. The treatment
ladder extends to step 5, however potential participants on this step would have met the exclusion criteria for unstable asthma. This table suggests a slight difference between the groups with the comparison group possibly being on higher doses of ICS to start with, and using less reliever inhaler. The comparison group also report taking more of their prescribed ICS dose than the intervention group. Few participants had been prescribed oral prednisolone in the preceding 12 months, therefore using mean or median to describe this variable was not helpful and the proportion being prescribed at least one course in the last 12 months was used instead.

Table 6.7 Asthma diagnosis and medications, data is either n (%), or median (IQR)

<table>
<thead>
<tr>
<th></th>
<th>Overall (n = 51)</th>
<th>Comparison (n = 26 )</th>
<th>Intervention (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of asthma diagnosis (yrs)</td>
<td>18.5 (8.6 to 28.6)</td>
<td>17.0 (8.6 to 27.8)</td>
<td>20.3 (9.7 to 28.6)</td>
</tr>
<tr>
<td>Family history of asthma</td>
<td>38 (75)</td>
<td>18 (70)</td>
<td>20 (80)</td>
</tr>
<tr>
<td>BTS/SIGN treatment level:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step 1</td>
<td>2 (4)</td>
<td>0 (0)</td>
<td>2 (8)</td>
</tr>
<tr>
<td>Step 2</td>
<td>20 (39)</td>
<td>9 (35)</td>
<td>11 (44)</td>
</tr>
<tr>
<td>Step 3</td>
<td>20 (40)</td>
<td>12 (46)</td>
<td>8 (32)</td>
</tr>
<tr>
<td>Step 4</td>
<td>9 (18)</td>
<td>5 (19)</td>
<td>4 (16)</td>
</tr>
<tr>
<td>Equivalent beclometasone dose (mcg per day)</td>
<td>400 (400 to 1000)</td>
<td>650 (400 to 800)</td>
<td>400 (200 to 1000)</td>
</tr>
<tr>
<td>Puffs of reliever inhaler used per average week</td>
<td>8 (4 to 20)</td>
<td>4 (2 to 12)</td>
<td>10 (4 to 28)</td>
</tr>
<tr>
<td>% prescribed ICS taken in average week</td>
<td>88 (50 to 100)</td>
<td>100 (50 to 100)</td>
<td>86 (25 to 100)</td>
</tr>
<tr>
<td>≥ 1 prednisolone course in last 12 months</td>
<td>16 (31)</td>
<td>9 (35)</td>
<td>7 (28)</td>
</tr>
</tbody>
</table>

ICS = inhaled corticosteroids
* Based on 50 participants (24/25 in intervention group), as one person not prescribed ICS

The number of contacts with health professionals is shown in Table 6.8. There were very few hospitalisations or visits to the emergency department in this group, therefore the data is presented as the proportion overall and per group with at least 1 event. Around a half of participants had seen their GP for their asthma out with the usual routine review. Only three participants had not attended for an asthma review in the preceding 12 months (all intervention group).
Table 6.8 Asthma related health service contacts in preceding 12 months, data is n (%)  

<table>
<thead>
<tr>
<th>Service Contact</th>
<th>Overall (n = 51)</th>
<th>Comparison (n = 26)</th>
<th>Intervention (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1 hospitalisations or ED visits</td>
<td>3 (6)</td>
<td>1 (4)</td>
<td>2 (8)</td>
</tr>
<tr>
<td>≥ 1 urgent GP visits</td>
<td>25 (49)</td>
<td>15 (58)</td>
<td>10 (40)</td>
</tr>
<tr>
<td>≥ 1 routine review</td>
<td>48 (94)</td>
<td>26 (100)</td>
<td>22 (88)</td>
</tr>
</tbody>
</table>

ED = emergency department. GP = general practitioner

6.4.4 Baseline questionnaire scores

The baseline questionnaire scores again demonstrate that the groups were well matched (Table 6.9). The ACQ shows these participants on average had uncontrolled asthma beyond the minimum requirement of ≥1, with mid-range quality of life scores. The intervention group appear to have lower MMAS scores (self-reported adherence measure) which is consistent with the lower reported percentage of ICS taken reported earlier, although interestingly this does not translate into any obvious differences in symptoms, QOL, or PAM scores.

Table 6.9 Baseline questionnaire scores, data are n (%), or median (IQR) unless otherwise stated

<table>
<thead>
<tr>
<th>Measure</th>
<th>Overall (n = 51)</th>
<th>Comparison (n = 26)</th>
<th>Intervention (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACQ mean (SD)</td>
<td>2.0 (0.6)</td>
<td>2.1 (0.7)</td>
<td>1.9 (0.6)</td>
</tr>
<tr>
<td>Mini-AQLQ mean (SD)</td>
<td>4.8 (1.0)</td>
<td>4.6 (1.0)</td>
<td>5.1 (1.0)</td>
</tr>
<tr>
<td>EQ-5D index (range 0 – 1.000)</td>
<td>0.796 (0.689 to 1.000)</td>
<td>0.796 (0.620 to 1.000)</td>
<td>0.848 (0.725 to 1.000)</td>
</tr>
<tr>
<td>EQ-5D VAS (range 0 – 100)</td>
<td>80 (70 to 85)</td>
<td>80 (70.0 to 90)</td>
<td>75 (70 to 84)</td>
</tr>
<tr>
<td>MMAS total score (range 0 – 8) mean (SD):</td>
<td>4.80 (1.91)</td>
<td>5.02 (2.14)</td>
<td>4.53 (1.61)</td>
</tr>
<tr>
<td>MMAS low adherence (score &lt;6)</td>
<td>26 (57.8)</td>
<td>12 (48)</td>
<td>14 (70)</td>
</tr>
<tr>
<td>Patient Activation Measure (PAM) (range 0 – 100), mean (SD)</td>
<td>66.3 (12.6)</td>
<td>66.8 (14)</td>
<td>65.8 (11)</td>
</tr>
<tr>
<td>Level 1</td>
<td>3 (6)</td>
<td>1 (4)</td>
<td>2 (8)</td>
</tr>
<tr>
<td>Level 2</td>
<td>5 (10)</td>
<td>4 (15)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Level 3</td>
<td>27 (53)</td>
<td>11 (42)</td>
<td>16 (64)</td>
</tr>
<tr>
<td>Level 4</td>
<td>16 (31)</td>
<td>10 (39)</td>
<td>6 (24)</td>
</tr>
</tbody>
</table>

ACQ = Asthma Control Questionnaire. AQLQ = Asthma Quality of Life Questionnaire. MMAS = Morisky Medication Adherence Scale. PAM = Patient Activation Measure, 1 is lowest, 4 is best. VAS = visual analogue scale.
6.4.5 Baseline spirometry

In order to measure true pre-bronchodilator spirometry, participants had to remain off certain inhalers for a specific number of hours prior to the measurement. We recorded this in 49 out of the 51 participants and found that 2 participants in total (4%), (1 in each group), had taken medication that could interfere with their spirometry. In addition, tests had to meet reproducibility criteria outlined in the methods section.

Of the 51 baseline visits completed, 32 met ATS/ERS acceptability standards, with no between group differences seen (Table 6.10). The reasons for the 19 not meeting ATS guidelines were primarily due to not meeting reproducibility criteria (n=16), with the remaining 3 having either taken medication which could have interfered with spirometry result (n=1), or the data was missing in error from the CRF (n=2). Achieving reproducibility targets was limited by the spirometry device we used. This only provided a graph and reproducibility figures after being connected to a separate laptop and transferring the data - a process which could take 5-10 minutes. Any second attempt would require starting from scratch again with a minimum of three measures again. Given that ATS recommend a maximum of 8 measures in one sitting, we really only had two chances to get the reproducibility figures required.

<table>
<thead>
<tr>
<th>ATS standard Met</th>
<th>Total (n= 51)</th>
<th>Comparison (n = 26)</th>
<th>Intervention (n = 25)</th>
<th>p – value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>32 (63)</td>
<td>15 (58)</td>
<td>17 (68)</td>
<td>0.565</td>
</tr>
<tr>
<td>No</td>
<td>19 (37)</td>
<td>11 (42)</td>
<td>7 (32)</td>
<td></td>
</tr>
</tbody>
</table>

* Fisher’s Exact Test

The spirometry results for these 32 participants is shown in Table 6.11. This shows the groups were well matched. The overall mean FEV₁/FVC ratio was 76.0%, over the 70% cut off considered to reflect obstructive airway diseases such as asthma. This does not reflect misdiagnosis as often spirometry is normal between exacerbations in asthma [4].
Table 6.11 Baseline spirometry of those meeting ATS/ERS acceptability criteria, data are mean (SD) unless otherwise (n=32).

<table>
<thead>
<tr>
<th></th>
<th>Overall (n = 32)</th>
<th>Comparison (n = 15)</th>
<th>Intervention (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁ (L)</td>
<td>2.58 (0.59)</td>
<td>2.51 (0.64)</td>
<td>2.66 (0.55)</td>
</tr>
<tr>
<td>FEV₁ % predicted</td>
<td>83.8 (14.2)</td>
<td>82.0 (15.5)</td>
<td>85.8 (12.9)</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>3.42 (0.71)</td>
<td>3.36 (0.70)</td>
<td>3.48 (0.74)</td>
</tr>
<tr>
<td>FEV₁/FVC *100</td>
<td>75.9 (9.1)</td>
<td>75.0 (11.0)</td>
<td>76.9 (6.5)</td>
</tr>
<tr>
<td>PEF (L/min) (via spirometry)</td>
<td>408 (94)</td>
<td>399 (87)</td>
<td>417 (105)</td>
</tr>
</tbody>
</table>

FEV₁ = forced expiratory volume in 1 second. FVC = forced vital capacity. PEF = peak expiratory flow.

The full 51 baseline spirometry measures are shown in Table 6.12, which shows similar results to those achieving acceptability criteria.

Table 6.12 Baseline lung function and inflammation results of all participants, data are mean (SD) unless otherwise (n=51)

<table>
<thead>
<tr>
<th></th>
<th>Overall (n = 51)</th>
<th>Comparison (n = 26)</th>
<th>Intervention (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁ (L)</td>
<td>2.51 (0.69)</td>
<td>2.46 (0.75)</td>
<td>2.56 (0.64)</td>
</tr>
<tr>
<td>FEV₁ % predicted</td>
<td>82.7 (14.4)</td>
<td>81.1 (14.6)</td>
<td>84.4 (14.4)</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>3.40 (0.99)</td>
<td>3.28 (0.91)</td>
<td>3.61 (1.07)</td>
</tr>
<tr>
<td>FEV₁/FVC *100</td>
<td>74.3 (11.0)</td>
<td>75.3 (10.0)</td>
<td>73.1 (12.5)</td>
</tr>
<tr>
<td>PEF (L/min) (via spirometry)</td>
<td>389 (108)</td>
<td>390 (101)</td>
<td>388 (116)</td>
</tr>
</tbody>
</table>

FEV₁ = forced expiratory volume in 1 second. FVC = forced vital capacity. PEF = peak expiratory flow.

As this was pilot study we were interested in how feasible it was to measure spirometry in participants own homes, using a hand held device. In this study those not meeting ATS criteria were technically considered to be missing data.

6.4.6 Fractional exhaled Nitric Oxide (FeNO)

Table 6.13 reports the baseline FeNO results, which is a measure of lung inflammation. The low/normal FeNO may seem slightly at odds with the ACQ which indicated a lack of control. This could be explained by the fact that 50/51 (98%) were on ICS at baseline and median self-report adherence was 88%, as those taking ICS are known to have lower FeNO scores.
Table 6.13 Baseline Fractional exhaled Nitric Oxide (FeNO) results, data are median and IQR

<table>
<thead>
<tr>
<th></th>
<th>Overall (n = 51)</th>
<th>Comparison (n = 26)</th>
<th>Intervention (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FeNO (ppb)</td>
<td>26</td>
<td>26</td>
<td>26</td>
</tr>
<tr>
<td>median (IQR)</td>
<td>(13 to 45)</td>
<td>(11 to 38)</td>
<td>(19 to 45)</td>
</tr>
</tbody>
</table>

FeNO = fractional exhaled nitric oxide. IQR = interquartile range. ppb = parts per billion.

6.4.7 Missing data

There was minimal missing data. On two occasions, the information about whether participants had taken relevant inhalers prior to their spirometry was missing, as described above. With regards to the mini-AQLQ, one participant (ID17) had a missing response for 1 question at visit 2. This was managed using the recommended method of interpolating (pro-rata) missing values. There was one questionnaire response from MMAS missing from one participant (ID56). As per MMAS guidelines, the median value for that question was used. This was well within the 75% completion criterion for this questionnaire to be considered valid. Finally, there was one response missing for one participant for the PAM score (ID 53). This was managed as recommended by PAM literature where the total score is divided by the number of answers available, and then multiplied by the number of questions (13).

6.5 Results: Primary outcomes

6.5.1 Primary outcome1: Recruitment and retention

6.5.1.1 Flow of participants

The flow of participants through the study is outlined in Figure 6.1
Figure 6.1 Flow of participants through study

20 Practices NHS Greater Glasgow & Clyde (population 129,986)
• ≥ 16 age
• diagnosis asthma *

Postal invites sent = 5383 (4.1%)

No response = 4890
Negative response = 247

Positive responses = 246 (4.6%)

Not contacted = 61
• Unable to = 33
• Received after target reached = 28

Telephone screening = 185 (75.2%)

Not eligible = 121
• ACQ <1 = 90
• No internet = 10
• Other lung disease = 9
• Unstable asthma = 7

Baseline visit booked = 64 (34.6%)

Baseline visit not completed = 13
• ACQ <1 = 2
• Unstable asthma = 1
• Changed mind/ lost contact = 10

Recruited to study and randomised = 51 (0.95% of those invited)
Researcher takes informed consent, socio-demographics, general medical history, including current medications, questionnaires, spirometry, FeNO.

Intervention Group n = 25
12 weeks access to intervention. Provided with login details and brief introduction to resource

Visit 2 completed n = 20/25 (80%)
Unavailable for visit = 5

Control group n = 26
Usual care for 12 weeks

Visit 2 completed = 25/26 (96%)
Unable to contact = 1
Access to the intervention (if desired)
6.5.1.2 Recruitment from Primary Care

I coordinated recruitment aided by my colleague KS and the SPCRN. We sent 5383 invites from 20 practices across Greater Glasgow and Clyde health board areas, with one practice population receiving a second follow up mailing. These practices along with list sizes and deprivation percentages are shown in Table 6.14. The even spread of deprivation across the 20 participating practices is shown in Figure 6.2.

Recruitment to previous asthma studies has been very challenging, so in order to detect if there were similar issues with this trial I planned monthly recruitment updates. Based on previous experience I calculated how many positive responses I should be aiming for in order to meet recruitment targets, and then tracked the positive responses as they arrived. This is illustrated in the graph below (Figure 6.3), and shows that our initial response was poorer than anticipated, but then caught up and exceeded the target.
<table>
<thead>
<tr>
<th>Practice Code</th>
<th>List size *</th>
<th>% practice population deprived †</th>
<th>% of list size mailed</th>
<th>Invites posted</th>
<th>Date invites posted</th>
<th>Randomised</th>
<th>% of mailing randomised</th>
<th>% practice list randomised</th>
</tr>
</thead>
<tbody>
<tr>
<td>52382</td>
<td>3049</td>
<td>31.30</td>
<td>7.2%</td>
<td>221</td>
<td>01/05/13</td>
<td>5</td>
<td>2.3%</td>
<td>0.16%</td>
</tr>
<tr>
<td>40008</td>
<td>6439</td>
<td>14.94</td>
<td>3.0%</td>
<td>192</td>
<td>29/07/13</td>
<td>2</td>
<td>1.0%</td>
<td>0.03%</td>
</tr>
<tr>
<td>52330</td>
<td>4000</td>
<td>67.68</td>
<td>7.4%</td>
<td>297</td>
<td>14/08/13</td>
<td>2</td>
<td>0.7%</td>
<td>0.05%</td>
</tr>
<tr>
<td>49681</td>
<td>8341</td>
<td>5.09</td>
<td>4.4%</td>
<td>371</td>
<td>03/09/13</td>
<td>2</td>
<td>0.5%</td>
<td>0.02%</td>
</tr>
<tr>
<td>87112</td>
<td>6567</td>
<td>0.01</td>
<td>5.8%</td>
<td>382</td>
<td>30/10/13</td>
<td>6</td>
<td>1.6%</td>
<td>0.09%</td>
</tr>
<tr>
<td>43538</td>
<td>2149</td>
<td>69.94</td>
<td>8.9%</td>
<td>191</td>
<td>30/10/13</td>
<td>3</td>
<td>1.6%</td>
<td>0.14%</td>
</tr>
<tr>
<td>40116</td>
<td>4102</td>
<td>51.66</td>
<td>5.7%</td>
<td>234</td>
<td>15/11/13</td>
<td>1</td>
<td>0.4%</td>
<td>0.02%</td>
</tr>
<tr>
<td>43576 ‡</td>
<td>21620</td>
<td>22.35</td>
<td>2.3%</td>
<td>493</td>
<td>01/12/13</td>
<td>1</td>
<td>0.2%</td>
<td>0.00%</td>
</tr>
<tr>
<td>40121</td>
<td>5209</td>
<td>10.17</td>
<td>4.1%</td>
<td>211</td>
<td>03/12/13</td>
<td>6</td>
<td>2.8%</td>
<td>0.12%</td>
</tr>
<tr>
<td>49074</td>
<td>2620</td>
<td>48.62</td>
<td>3.8%</td>
<td>100</td>
<td>03/12/13</td>
<td>0</td>
<td>0.0%</td>
<td>0.00%</td>
</tr>
<tr>
<td>40031</td>
<td>4448</td>
<td>8.03</td>
<td>1.5%</td>
<td>65</td>
<td>04/12/13</td>
<td>0</td>
<td>0.0%</td>
<td>0.00%</td>
</tr>
<tr>
<td>40046</td>
<td>8971</td>
<td>38.80</td>
<td>5.0%</td>
<td>448</td>
<td>03/01/14</td>
<td>3</td>
<td>0.7%</td>
<td>0.03%</td>
</tr>
<tr>
<td>49642</td>
<td>6593</td>
<td>29.75</td>
<td>5.9%</td>
<td>391</td>
<td>03/01/14</td>
<td>8</td>
<td>2.0%</td>
<td>0.12%</td>
</tr>
<tr>
<td>42255</td>
<td>6550</td>
<td>36.63</td>
<td>3.8%</td>
<td>248</td>
<td>03/01/14</td>
<td>4</td>
<td>1.6%</td>
<td>0.06%</td>
</tr>
<tr>
<td>40210</td>
<td>1700</td>
<td>37.56</td>
<td>8.6%</td>
<td>146</td>
<td>16/01/14</td>
<td>0</td>
<td>0.0%</td>
<td>0.00%</td>
</tr>
<tr>
<td>43011</td>
<td>5992</td>
<td>55.17</td>
<td>4.1%</td>
<td>246</td>
<td>30/01/14</td>
<td>4</td>
<td>1.6%</td>
<td>0.07%</td>
</tr>
<tr>
<td>87471</td>
<td>7716</td>
<td>30.37</td>
<td>1.7%</td>
<td>133</td>
<td>30/01/14</td>
<td>0</td>
<td>0.0%</td>
<td>0.00%</td>
</tr>
<tr>
<td>43100</td>
<td>7529</td>
<td>4.15</td>
<td>4.9%</td>
<td>372</td>
<td>01/02/14</td>
<td>0</td>
<td>0.0%</td>
<td>0.00%</td>
</tr>
<tr>
<td>43576 ‡</td>
<td>21620</td>
<td>22.35</td>
<td>0.9%</td>
<td>200</td>
<td>01/02/14</td>
<td>3</td>
<td>1.5%</td>
<td>0.01%</td>
</tr>
<tr>
<td>87339</td>
<td>5012</td>
<td>24.66</td>
<td>2.6%</td>
<td>129</td>
<td>03/02/14</td>
<td>0</td>
<td>0.0%</td>
<td>0.00%</td>
</tr>
<tr>
<td>40140</td>
<td>11379</td>
<td>5.45</td>
<td>2.8%</td>
<td>313</td>
<td>03/02/14</td>
<td>1</td>
<td>0.3%</td>
<td>0.01%</td>
</tr>
</tbody>
</table>

* correct at time invites posted
† % practice population in lowest deprivation quintile, correct as of 18/2/15
‡ more targeted search criteria used in second mailing from same practice accounts for lower percentage of list size mailed.

| Total Mailings | 5383 | 51 |
While the positive response rate from the first practice was lower than anticipated (5.5%), there were 5 randomisations from it: 42% of positive responses, 2.3% of the mailing, and 0.16% of the practice list. This provided us with falsely optimistic recruitment projections, whereby if the following 3 practices had maintained this I would have expected to randomise 30 participants from them, whereas as Table 6.14 shows only 6 were randomised. The reasons why the first practice randomisation rate was so much higher than subsequent practices is not clear, and subsequently there was considerable variation across the practices with no obvious relationship to deprivation.

This lower than projected positive responses and randomisation was detected by September and a further drive to recruit more practices and send out more mailings was undertaken as a result. This is shown in Table 6.14, and illustrated visually in Figure 6.4.
As well as recognising that we needed to recruit more practices, I responded to this by reviewing the search criteria used to identify potential participants, with a view to making it more targeted. When refining search terms, beyond a certain number of limiters, I noted that the results of the search became less reliable and reproducible, becoming a particular issue once more than 6 search terms were used. The original search had 2 terms:

Asthma (active problem)
AND ≥ 16 years

By the final search this has been modified to:

Asthma (active problem)
AND ≥ 16 years
AND salbutamol inhaler (in preceding 8 months)
NOT Spiriva, tiotropium (COPD specific inhalers)
NOT oral prednisolone (current repeat medication)
NOT palliative care register.
Targeting the mailing in this way roughly halved the number of potential participants identified. Targeting the mailing in this way had two particular benefits. Firstly, it reduced the financial and time costs of preparing and posting mailing packs which were targeting patients who were unlikely to fulfil our requirements. It also reduced the size of the list of patients that GPs had to screen, thereby reducing their work and speeding the process up.

### 6.5.1.3 Other recruitment methods

All participants were recruited from primary care mailings. We had 1 telephone enquiry and 2 email enquiries from contacts of those who had been screened (snowballing technique) but none were ultimately eligible. We did not recruit anyone from posters, and we did not attempt to recruit from secondary care, or previous asthma participants.

### 6.5.1.4 Screening for eligibility

As we received positive responses my colleague KS and I screened them for eligibility over the telephone. We screened 185 potential participants, eventually randomising 51 (28%). On average, those who were randomised were more likely to be younger and more likely to be female, but importantly there was no difference in the deprivation category between those randomised versus those ineligible (Table 6.15).

#### Table 6.15 Screening data (n, % unless otherwise stated)

<table>
<thead>
<tr>
<th></th>
<th>Ineligible (n = 134)</th>
<th>Randomised (n=51)</th>
<th>p values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) * mean (SD)</td>
<td>51.5 (17.0)</td>
<td>45.5 (15.4)</td>
<td>0.03</td>
</tr>
<tr>
<td>Female (%)</td>
<td>50.0</td>
<td>74.5</td>
<td>0.03</td>
</tr>
<tr>
<td>SIMD quintile (1 most deprived, 5 least deprived)†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIMD 1</td>
<td>34 (27.9)</td>
<td>14 (27.5)</td>
<td></td>
</tr>
<tr>
<td>SIMD 2</td>
<td>22 (18.0)</td>
<td>11 (21.6)</td>
<td></td>
</tr>
<tr>
<td>SIMD 3</td>
<td>15 (12.3)</td>
<td>9 (17.6)</td>
<td>0.721</td>
</tr>
<tr>
<td>SIMD 4</td>
<td>20 (16.4)</td>
<td>5 (9.8)</td>
<td></td>
</tr>
<tr>
<td>SIMD 5</td>
<td>31 (25.4)</td>
<td>12 (23.5)</td>
<td></td>
</tr>
</tbody>
</table>

* Data for 177/185 individuals
† Scottish Index of Multiple Morbidity, data for 173/185 individuals

Of the 134 people who were not eligible to participate, the most common reason was that their ACQ was less than 1, i.e. they were not symptomatic enough. The full breakdown for reason for exclusion is shown in Table 6.16. Thirteen of
these 134 potential participants had originally passed the telephone screening stage, but weren’t randomised, for reasons outlined in Figure 6.1.

Table 6.16 Reason for exclusion (data available for 131/134 individuals)

<table>
<thead>
<tr>
<th>Reason for exclusion*</th>
<th>n (%)</th>
<th>Age yrs (mean, SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACQ score &lt;1</td>
<td>92 (70)</td>
<td>50 (17)</td>
</tr>
<tr>
<td>No internet access</td>
<td>10 (8)</td>
<td>73 (12)</td>
</tr>
<tr>
<td>Changed mind/unable to contact</td>
<td>10 (7)</td>
<td>39 (14)</td>
</tr>
<tr>
<td>Other lung disease</td>
<td>9 (7)</td>
<td>58 (9)</td>
</tr>
<tr>
<td>Unstable asthma</td>
<td>8 (6)</td>
<td>51 (15)</td>
</tr>
<tr>
<td>No Asthma, or symptoms &lt; 1 year</td>
<td>1 (1)</td>
<td>78</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>1 (1)</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Table 6.16 also shows the average age of the individuals per exclusion reason. This demonstrates that those who ‘changed their mind’ were younger in general. This usually happened when potential participants were willing and able to participate but we were unable to agree a date for arranging the study visits. Or occasionally we would arrange one or two visit dates and the participant would cancel repeatedly, often due to work or family commitments. The other main interesting finding is that those who were ineligible due to not having internet access appeared to be older than those ineligible for other reasons.

6.5.1.5 Attrition rates

In the intervention group, 5 of the 25 were not available for follow up visits (20%), and 1 out of 26 (4%) in the comparison group (shown earlier in Figure 6.1), so overall attrition was 12%. Reasons for loss to follow up in intervention group was mainly that participants appeared unavailable for follow up visits, rather than being unable to contact them at all. All 5 had not used the website and I speculate that they may have felt uncomfortable about this and preferred to avoid the second visit. This was despite reassurances that the follow up appointment was still very helpful to us. We were unable to contact the individual in the control group at all for a follow up visit.

6.5.2 Primary outcome 2: Website use

Table 6.17 provides some results about how the website was used. Twenty five participants were allocated to the intervention group and 19 of those logged on
(76%). This is comparable to the experiences of those in the expert panel working on a range of other health behaviour change websites, who had suggested about 75% of those allocated will log on (personal communication).

Out of the 19 who logged in, 17 went beyond the initial introduction module to reach the section where the website became specifically tailored. At this point users were asked to identify which one of 3 options they most identified with. The majority of people reported that they usually used their preventer as prescribed.

<table>
<thead>
<tr>
<th>Table 6.17 Website use by those who completed study, during study period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (% of eligible participants who logged in)</td>
</tr>
<tr>
<td>Mean number of logins (median, range)</td>
</tr>
<tr>
<td>Mean time spent logged in minutes (range)</td>
</tr>
</tbody>
</table>

Number choosing individual options (n = 17):

- I have never been prescribed a preventer inhaler: 1 (6%)
- I have been prescribed an inhaler but don’t really use it: 6 (35%)
- I have a preventer and usually use it as prescribed: 10 (59%)

Figure 6.5 illustrates the number of log ins and total time spent on the website for the 20 participants who completed the study and suggests that those who logged in more than once tended to use the website overall for longer.
Figure 6.5 Total time logged in and number of logins per participant (in order of length of time on website)

Table 6.18 confirms that the majority of participants agreed that asthma impacted on their lives in some way.

Table 6.18 User responses regarding impact of asthma on life, n = 19.

<table>
<thead>
<tr>
<th>Questions asked by website:</th>
<th>Yes (n) *</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Does your asthma ever stop you doing things you would like to do? (exercising, working, gardening, housework, visiting friends for example)</td>
<td>10/19</td>
</tr>
<tr>
<td>2. Does it sometimes affect your sleep?</td>
<td>12/19</td>
</tr>
<tr>
<td>3. Do coughs and colds sometimes cause your asthma to flare up?</td>
<td>16/19</td>
</tr>
<tr>
<td>4. Do you often have to use your blue/reliever inhaler more than twice a week?</td>
<td>15/19</td>
</tr>
<tr>
<td>5. Have you had an asthma attack (e.g. needing steroid tablets) in the last 6 months?</td>
<td>1/19</td>
</tr>
</tbody>
</table>

Users ticking at least one limitation due to asthma (options 1-5 above) n (%) 18/19 (95)

* Users could choose more than one.

Table 6.19 lists how often the individual sections were visited and how long was spent there. Every section of the website was visited at least twice. Beyond the core ‘introduction’ and ‘my asthma’ sections the most popular sections were
'physical activity' and 'common concerns and queries'. 'Take the 4 week challenge' was also popular. It was visited 17 times, with 4 users completing the section and signing up to the 4 week challenge and 3 opting in to have email reminders. Although 2 users visited the stop smoking page, neither went on to subsequently register for the smoking cessation support.

![Table 6.19 How often different sections were visited and for how long](image)

<table>
<thead>
<tr>
<th>Topic</th>
<th>Total time spent (mins)</th>
<th>Number of visits to section *</th>
<th>Number of users visiting section</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction page (including home page) †</td>
<td>127.9</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>My Asthma (total) ‡</td>
<td>76.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No preventer</td>
<td>12.5</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Sometimes preventer</td>
<td>16.6</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Usually preventer</td>
<td>47.7</td>
<td>16</td>
<td>10</td>
</tr>
<tr>
<td>Treatments</td>
<td>17.1</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Asthma Reviews §</td>
<td>30.0</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Action Plans</td>
<td>19.4</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Physical Activity</td>
<td>46.0</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>Common concerns and queries</td>
<td>20.2</td>
<td>15</td>
<td>11</td>
</tr>
<tr>
<td>Stress &amp; Anxiety</td>
<td>6.0</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Take the 4 week Challenge</td>
<td>57.4</td>
<td>17</td>
<td>13</td>
</tr>
<tr>
<td>Like to stop smoking ‖</td>
<td>1.0</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Useful info and links</td>
<td>22.7</td>
<td>11</td>
<td>9</td>
</tr>
</tbody>
</table>

* most number of visits to the introduction pages of a section
† Users were tunnelled through these sections at initial login
‡ Users had to chose one of three options to progress through this section
§ 6 users visited quiz within this section
‖ This section only consisted of 1 page which linked to an external smoking cessation website, also developed using LifeGuide software.

6.5.2.1 Website users compared to non-users

This section presents results on all of those allocated to the intervention (n=25) not just the 20 participants who completed the study. These results are shown in Table 6.20. Nine out of the 25 intervention group participants could be classed as non-users (6 of whom didn’t use it at all). There does seem to be a suggestion that non-users while more likely to be from a deprived area, were overall experiencing better controlled asthma, and enjoyed higher quality of life scores (none of which was statistically significant). They did have statistically significantly higher MMAS scores indicating as a group they were more likely to take their medication. This perhaps implies less need for such a resource.
Table 6.20 Website users compared to non-users at baseline, data are n(%) unless otherwise stated

<table>
<thead>
<tr>
<th></th>
<th>Non-users (n = 9)</th>
<th>Users (n = 16)</th>
<th>p values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years (mean, SD)</td>
<td>46.4 (16.6)</td>
<td>43.6 (17.4)</td>
<td>0.688</td>
</tr>
<tr>
<td>Female</td>
<td>7 (78)</td>
<td>11 (69)</td>
<td>1.000</td>
</tr>
<tr>
<td>SIMD quintile (1 = most deprived, 5 = least deprived)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>4 (44)</td>
<td>3 (19)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2 (22)</td>
<td>3 (19)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1 (11)</td>
<td>4 (25)</td>
<td>0.683</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>2 (13)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2 (22)</td>
<td>4 (25)</td>
<td></td>
</tr>
<tr>
<td>ACQ at v1</td>
<td>1.69 (0.57)</td>
<td>2.00 (0.56)</td>
<td>0.205</td>
</tr>
<tr>
<td>mini-AQLQ at v1</td>
<td>5.46 (0.66)</td>
<td>4.83 (1.07)</td>
<td>0.084</td>
</tr>
<tr>
<td>MMAS at v1</td>
<td>5.4 (1.4)</td>
<td>4.0 (1.6)</td>
<td><strong>0.034</strong></td>
</tr>
</tbody>
</table>

ACQ = asthma control questionnaire. AQLQ = asthma quality of life questionnaire. MMAS = morisky medication adherence score. SIMD = scottish index of multiple deprivation. v1 = visit 1.

6.5.3 Primary outcome 3: Asthma Control Questionnaire (ACQ)

My first clinical primary outcome was the 7 question ACQ, and baseline scores between the two groups were well matched. Baseline adjusted analysis showed the mean ACQ in the intervention group was lower (desirable) than the comparison group by 0.42 (95% CI -0.11 to 0.95) at follow up. This was not statistically significant, with full details shown in Table 6.21 below. I have presented the results graphically in Figure 6.6 below.

Table 6.21 ACQ 7 question version score (n = 45)

<table>
<thead>
<tr>
<th></th>
<th>Baseline Mean (SD)</th>
<th>Followup Mean (SD)</th>
<th>Change Mean (SD)</th>
<th>Estimated difference (a) (95% CI), p – value (Intervention – Comparison)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACQ (range 0 – 6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>1.89 (0.57)</td>
<td>1.23 (0.80)</td>
<td>-0.65 (0.92)</td>
<td>-0.42 (-0.95 to 0.11),</td>
</tr>
<tr>
<td>Comparison</td>
<td>2.08 (0.66)</td>
<td>1.78 (1.06)</td>
<td>-0.30 (0.85)</td>
<td>0.121</td>
</tr>
</tbody>
</table>

(a) Regression model estimate of difference between groups in the mean change in outcome, adjusting for baseline value.
The minimally important difference (MID) [176] is a reduction of 0.5 or more.

Table 6.22 shows that for 55% in the intervention group, ACQ score decreased by 0.5, compared to 48% in the comparison group, not statistically significant.

<table>
<thead>
<tr>
<th></th>
<th>Comparison (n = 25)</th>
<th>Intervention (n = 20)</th>
<th>Between group p value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACQ &lt; MID</td>
<td>13 (52)</td>
<td>9 (45)</td>
<td>0.767</td>
</tr>
<tr>
<td>ACQ ≥ MID</td>
<td>12 (48)</td>
<td>11 (55)</td>
<td></td>
</tr>
</tbody>
</table>

* Fishers exact test

All participants in the study had an ACQ ≥ 1 at baseline. Table 6.23 shows that by follow up 45% in the intervention group compared to 24% in the comparison group had a score of <1, i.e. they had moved from ‘uncontrolled’ to ‘controlled’.

<table>
<thead>
<tr>
<th></th>
<th>Comparison (n = 25)</th>
<th>Intervention (n = 20)</th>
<th>Between group p value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACQ &lt; 1 at v2</td>
<td>6 (24)</td>
<td>9 (45)</td>
<td>0.205</td>
</tr>
<tr>
<td>ACQ ≥ 1 at v2</td>
<td>19 (76)</td>
<td>11 (55)</td>
<td></td>
</tr>
</tbody>
</table>

* Fishers exact test
Due to the high number of spirometry not meeting ATS criteria, I also analysed the equally valid 6 question version of the ACQ [198], as this does not include a spirometry related item, and found a similar result.

| Table 6.24 ACQ 6 item version scores (e.g no spirometry measure) (n = 45) |
|------------------|------------------|------------------|------------------|------------------|
|                  | Baseline Mean (SD) | Followup Mean (SD) | Change Mean (SD) | Estimated difference * (95%CI), p – value |
| ACQ (range 0 – 6) |                   |                   |                  |                                       |
| Intervention     | 1.87 (0.59)       | 1.22 (0.91)       | -0.65 (1.08)     | -0.36 (-0.96 to 0.23), 0.225          |
| Comparison       | 1.97 (0.68)       | 1.65 (1.15)       | -0.32 (0.94)     |                                       |

* Regression model estimate of difference between groups in the mean change in outcome, adjusting for baseline value

The MID results for the 6 question version are the same as for the 7 question version, as reported previously in Table 6.22.

**6.5.4 Primary outcome 4: Mini Asthma Quality of Life Questionnaire (AQLQ) score**

Our second clinical primary outcome was the 15 item mini AQLQ. Baseline adjusted analysis showed the mean mini-AQLQ score in the intervention group was higher (desirable) than the comparison group by 0.38 (95% CI -0.13 to 0.89) (Table 6.25) at follow up.

The scores were then analysed for the 4 individual domains (Table 6.25 also). This shows that the activity limitation domain was both statistically and clinically significantly improved in the intervention group at follow up, with all other domains trending in the direction of favouring the intervention, with the symptom domain difference reaching clinical but not quite statistical significance.
Table 6.25 Mini-AQLQ total and individual domain scores

<table>
<thead>
<tr>
<th>Mini-AQLQ total score (range 1 – 7)</th>
<th>Baseline Mean (SD)</th>
<th>Followup Mean (SD)</th>
<th>Change Mean (SD)</th>
<th>Estimated difference* (95%CI), p – value (Intervention – Comparison)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mini-AQLQ</td>
<td>Intervention</td>
<td>4.97 (1.03)</td>
<td>5.40 (1.01)</td>
<td>0.43 (0.78)</td>
</tr>
<tr>
<td></td>
<td>Comparison</td>
<td>4.65 (1.02)</td>
<td>4.76 (1.30)</td>
<td>0.11 (0.88)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mini-AQLQ Individual Domains Scores (range 1 – 7)</th>
<th>Baseline Mean (SD)</th>
<th>Followup Mean (SD)</th>
<th>Change Mean (SD)</th>
<th>Estimated difference* (95%CI), p – value (Intervention – Comparison)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom</td>
<td>Intervention</td>
<td>4.56 (1.10)</td>
<td>5.15 (1.20)</td>
<td>0.59 (1.10)</td>
</tr>
<tr>
<td></td>
<td>Comparison</td>
<td>4.30 (0.84)</td>
<td>4.38 (1.35)</td>
<td>0.08 (1.05)</td>
</tr>
<tr>
<td>Activity limitation</td>
<td>Intervention</td>
<td>5.30 (1.24)</td>
<td>5.98 (0.92)</td>
<td>0.68 (1.01)</td>
</tr>
<tr>
<td></td>
<td>Comparison</td>
<td>5.31 (1.33)</td>
<td>5.38 (1.33)</td>
<td>0.07 (1.10)</td>
</tr>
<tr>
<td>Emotional function</td>
<td>Intervention</td>
<td>5.48 (1.09)</td>
<td>5.75 (1.01)</td>
<td>0.27 (0.78)</td>
</tr>
<tr>
<td></td>
<td>Comparison</td>
<td>4.80 (1.48)</td>
<td>4.84 (1.82)</td>
<td>0.04 (1.30)</td>
</tr>
<tr>
<td>Environmental Stimuli</td>
<td>Intervention</td>
<td>4.75 (1.39)</td>
<td>4.85 (1.30)</td>
<td>0.10 (0.89)</td>
</tr>
<tr>
<td></td>
<td>Comparison</td>
<td>4.11 (1.54)</td>
<td>4.23 (1.67)</td>
<td>0.12 (0.90)</td>
</tr>
</tbody>
</table>

* Regression model estimate of difference between groups in the mean change in outcome, adjusting for baseline value. AQLQ = Asthma Quality of Life Questionnaire

Fifty percent of participants in the intervention group compared to 35% in the comparison group achieved the MID, again not statistically significant as shown in Table 6.26.

Table 6.26 Proportion with mini-AQLQ improvement ≥0.5 (MID) at follow up, data are n (%)

<table>
<thead>
<tr>
<th></th>
<th>Comparison (n = 25)</th>
<th>Intervention (n = 20)</th>
<th>Between group p value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>mini-AQLQ &lt; MID</td>
<td>16 (64)</td>
<td>10 (50)</td>
<td>0.379</td>
</tr>
<tr>
<td>mini-AQLQ ≥ MID</td>
<td>9 (36)</td>
<td>10 (50)</td>
<td></td>
</tr>
</tbody>
</table>

* Fisher’s Exact Test

6.6 Results: Secondary outcomes

6.6.1 EQ-5D

There was no difference in the change in EQ5D health utility scores between groups (p = 0.972) as shown in Table 6.27.
The second part of the EQ-5D is the visual analogue scale (VAS). This asks participants to rate their health ‘today’ (i.e. day they are filling out the scale) from 0 (worst possible) to 100 (best imaginable). The median difference in the score at follow up in the intervention group was 2.5, compared to 1.0 in the in comparison group (p = 0.409) as outlined in Table 6.27.

<table>
<thead>
<tr>
<th></th>
<th>Baseline Median (IQR)</th>
<th>Follow up Median (IQR)</th>
<th>Change Median (IQR)</th>
<th>p – value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EQ-5D Health Utility</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>0.848 (0.725 to 1.000)</td>
<td>1.000 (0.796 to 1.000)</td>
<td>0.000 (0.000 to 0.111)</td>
<td>0.972</td>
</tr>
<tr>
<td>Comparison</td>
<td>0.796 (0.620 to 1.000)</td>
<td>0.796 (0.727 to 1.000)</td>
<td>0.0000 (-0.052 to 0.194)</td>
<td>0.409</td>
</tr>
<tr>
<td><strong>EQ-5D VAS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>75 (70 to 84)</td>
<td>80 (73 to 88)</td>
<td>2.5 (-6.5 to 13.0)</td>
<td>0.409</td>
</tr>
<tr>
<td>Comparison</td>
<td>80 (70 to 90)</td>
<td>80 (70 to 90)</td>
<td>1.0 (-10 to 10)</td>
<td></td>
</tr>
</tbody>
</table>

* Wilcoxon test on change in scores (v2 – v1)

### 6.6.2 Patient Activation Measure (PAM)

The PAM score ranges from 0 to 100, and a high score is desirable indicating a patient is highly activated in relation to managing their own health. Baseline adjusted analysis showed that the mean difference in the score in the intervention was an improvement of 7.72 (95%CI 0.53 to 14.90, p value 0.036).

<table>
<thead>
<tr>
<th></th>
<th>Baseline mean (SD)</th>
<th>Followup mean (SD)</th>
<th>Change mean (SD)</th>
<th>Estimated difference * (95%CI), p – value (Intervention – Comparison)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PAM score (range 0-100)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>65.7 (10.0)</td>
<td>73.0 (13.9)</td>
<td>7.3 (11.3)</td>
<td>7.72 (0.53 to 14.90)</td>
</tr>
<tr>
<td>Comparison</td>
<td>66.2 (14.1)</td>
<td>65.7 (16.5)</td>
<td>-0.5 (12.5)</td>
<td>0.036</td>
</tr>
</tbody>
</table>

* Regression model estimate of difference between groups in the mean change in outcome, adjusting for baseline value

This individual PAM activation score can be used to stratify individuals into one of 4 levels as outlined in Table 6.29. The numbers in each individual level are small but there is a suggestion that those in the intervention group moved up
from level 3 to level 4, more than the comparison group, although it is worth noting there were more in the comparison group at level 4 at baseline.

Table 6.29 PAM activation levels per group

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n,%)</th>
<th>Follow up (n,%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Comparison</strong></td>
<td></td>
<td><strong>Intervention</strong></td>
</tr>
<tr>
<td><strong>Level 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disengaged and</td>
<td>1 (4.0)</td>
<td>1 (5.0)</td>
</tr>
<tr>
<td>overwhelmed</td>
<td>2 (8.0)</td>
<td>1 (5.0)</td>
</tr>
<tr>
<td><strong>Level 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Becoming aware</td>
<td>4 (16.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>but still</td>
<td>4 (16.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>struggling</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td><strong>Level 3</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taking action</td>
<td>11 (44.0)</td>
<td>16 (80.0)</td>
</tr>
<tr>
<td></td>
<td>11 (44.0)</td>
<td>8 (40.0)</td>
</tr>
<tr>
<td><strong>Level 4</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maintaining</td>
<td>9 (36.0)</td>
<td>3 (15.0)</td>
</tr>
<tr>
<td>behaviour,</td>
<td>8 (32.0)</td>
<td>11 (55.0)</td>
</tr>
<tr>
<td>pushing further</td>
<td>11 (55.0)</td>
<td>11 (55.0)</td>
</tr>
</tbody>
</table>

Another way of presenting this data is to look at the score at visit 1, and score at visit 2 and show the change per group (Table 6.30). This shows visually that more participants in the intervention group changed up a level (n=8). Where in the comparison group there was change in both directions, with 4 participants moving up, and 6 dropping down a level.

Table 6.30 PAM level change per group, data are n%

<table>
<thead>
<tr>
<th></th>
<th>Comparison group (n=25)</th>
<th>Intervention group (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>v1</td>
<td>v2</td>
<td>Level 1</td>
</tr>
<tr>
<td>Level 1</td>
<td>1 (4)</td>
<td></td>
</tr>
<tr>
<td>Level 2</td>
<td>1 (4)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Level 3</td>
<td>2 (8)</td>
<td>7 (28)</td>
</tr>
<tr>
<td>Level 4</td>
<td>1 (4)</td>
<td>2 (8)</td>
</tr>
</tbody>
</table>

Greyed out boxes are no change in level between visits

This data is summarised in Table 6.31, showing more in the intervention group moved up a level (40%), than in the comparison group (16%) (p = 0.096).
### Table 6.31 Participants who moved up an activation level by visit 2, data are n (%)

<table>
<thead>
<tr>
<th></th>
<th>Comparison (n = 25)</th>
<th>Intervention (n = 20)</th>
<th>p – value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No increase in PAM Level</td>
<td>21 (84)</td>
<td>12 (60)</td>
<td>0.096</td>
</tr>
<tr>
<td>Increase in PAM level</td>
<td>4 (16)</td>
<td>8 (40)</td>
<td></td>
</tr>
</tbody>
</table>

* Fisher’s Exact Test

### 6.6.3 Morisky Medication Adherence Scale (MMAS)

As reported earlier the baseline adherence data may suggest the intervention group had lower adherence at the start. By follow up, baseline adjusted analysis showed mean MMAS score in the intervention group was higher than in the comparison group by 0.19 (95% CI -0.50 to 0.88, p = 0.586), (Table 6.32). However, looking at the scores per group these show the intervention group improved more than the comparison group (0.58 vs 0.23) but had lower scores at baseline, therefore this may represent regression to the mean.

### Table 6.32 MMAS Total score (max = 8 = high adherence)

<table>
<thead>
<tr>
<th>MMAS total score (range 0-8)</th>
<th>Baseline Mean (SD)</th>
<th>Followup Mean (SD)</th>
<th>Change Mean (SD)</th>
<th>Estimated difference * (95%CI), p – value (intervention – comparison)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>4.88 (1.97)</td>
<td>5.46 (1.80)</td>
<td>0.58 (1.37)</td>
<td>0.19 (-0.50 to 0.88)</td>
</tr>
<tr>
<td>Comparison</td>
<td>5.59 (1.85)</td>
<td>5.82 (1.85)</td>
<td>0.23 (1.03)</td>
<td>p = 0.586</td>
</tr>
</tbody>
</table>

* Regression model estimate of difference between groups in the mean change in outcome, adjusting for baseline value

If I look specifically at those who did improve by 2 or more, (i.e. the proportion who achieved the MID) then Table 6.33 shows that 30% in the intervention group achieved this compared to only 4% in the comparison group (p = 0.034).

### Table 6.33 MMAS score improvement ≥ 2, n (%)

<table>
<thead>
<tr>
<th></th>
<th>Comparison (n = 25)</th>
<th>Intervention (n = 20)</th>
<th>p – value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMAS score change &lt; 2</td>
<td>24 (96)</td>
<td>14 (70)</td>
<td></td>
</tr>
<tr>
<td>MMAS score change ≥ 2</td>
<td>1 (4)</td>
<td>6 (30)</td>
<td>0.034</td>
</tr>
</tbody>
</table>

* Fisher’s Exact Test
6.6.4 Problematic experiences of therapy scale (PETS)

PETS aims to facilitate understanding of what barriers there are to using an intervention. This can be reported two ways. Firstly, as shown in Table 6.34, the mean score for each domain can be calculated, and the median score (IQR) for each domain presented.

<table>
<thead>
<tr>
<th>Domain</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms too severe to follow website advice, or symptoms aggravated</td>
<td>1.0 (1.0 to 1.0)</td>
</tr>
<tr>
<td>by website advice</td>
<td></td>
</tr>
<tr>
<td>Uncertain how to follow the website advice</td>
<td>1.0 (1.0 to 2.0)</td>
</tr>
<tr>
<td>Doubt about personal relevance of website advice</td>
<td>1.0 (1.0 to 1.7)</td>
</tr>
<tr>
<td>Practical obstacles to following website advice (e.g. time, opportunity)</td>
<td>3.3 (2.0 to 4.0)</td>
</tr>
</tbody>
</table>

1 = strongly disagree with statement, 5 = strongly agree with statement

The lowest possible score for each domain is 1 and corresponds to strongly disagreeing with the statements. Reassuringly the majority of people disagreed with statements relating to the first 3 domains. However, where people started to agree more strongly was when identifying practical barriers to using the intervention such as time and opportunity.

Another way of displaying the results of PETS is to look at the proportion of people who identified any barrier at all to using the intervention within a given domain, as shown in Table 6.35, confirming again that the biggest barriers are related to time and opportunity.

<table>
<thead>
<tr>
<th>Any barriers identified i.e agree or agree strongly with statement describing barriers (n = 19)</th>
<th>Any barriers n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms too severe to follow website advice, or symptoms aggravated by website advice</td>
<td>4 (21)</td>
</tr>
<tr>
<td>Uncertain how to follow the website advice</td>
<td>7 (37)</td>
</tr>
<tr>
<td>Doubt about personal relevance of website advices</td>
<td>8 (41)</td>
</tr>
<tr>
<td>Practical obstacles to following website advice (e.g. time, opportunity)</td>
<td>18 (95)</td>
</tr>
</tbody>
</table>
6.6.5 Lung function results

Out of the 45 participants who completed, 22 participants had spirometry tests meeting ATS criteria at both baseline and follow up visits, with no significant differences between treatment groups (Table 6.36), with 11 in each group. Of the 23 who didn’t meet criteria, not meeting reproducibility was the most common reason (n=21) with either medication taken prior to spirometry (n=3) or the data was missing from either visit 1 or visit 2 (n=2), with some participants having more than one reason for failing.

Table 6.36 Achieving ATS standard spirometry

<table>
<thead>
<tr>
<th>Achieved ATS standard</th>
<th>Comparison (n = 25)</th>
<th>Intervention (n = 20)</th>
<th>p – value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achieved ATS standard</td>
<td>11 (44)</td>
<td>11 (55)</td>
<td>0.554</td>
</tr>
<tr>
<td>Not achieving ATS standard</td>
<td>14 (56)</td>
<td>9 (45)</td>
<td></td>
</tr>
</tbody>
</table>

* Fisher’s Exact Test

The results from spirometry for the 22 meeting acceptability criteria are shown below (Table 1.36). This demonstrates that while trends favoured the intervention group, there were no statistically significant results.
### Table 6.37 Spirometry results (n=22)

<table>
<thead>
<tr>
<th></th>
<th>Baseline Mean (SD)</th>
<th>Followup Mean (SD)</th>
<th>Change Mean (SD)</th>
<th>Estimated difference* (95%CI), p – value (Intervention – comparison)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FEV(_1)</strong> (L)</td>
<td>Intervention</td>
<td>2.62 (0.56)</td>
<td>2.72 (0.58)</td>
<td>0.10 (0.18)</td>
</tr>
<tr>
<td></td>
<td>Comparison</td>
<td>2.66 (0.69)</td>
<td>2.68 (0.49)</td>
<td>0.02 (0.31)</td>
</tr>
<tr>
<td><strong>FEV(_1)</strong> % predicted</td>
<td>Intervention</td>
<td>87.4 (13.6)</td>
<td>90.6 (13.8)</td>
<td>3.3 (6.3)</td>
</tr>
<tr>
<td></td>
<td>Comparison</td>
<td>85.2 (17.1)</td>
<td>85.7 (11.9)</td>
<td>0.6 (9.4)</td>
</tr>
<tr>
<td><strong>FVC</strong> (L)</td>
<td>Intervention</td>
<td>3.44 (0.76)</td>
<td>3.47 (0.79)</td>
<td>0.02 (0.15)</td>
</tr>
<tr>
<td></td>
<td>Comparison</td>
<td>3.44 (0.72)</td>
<td>3.27 (0.62)</td>
<td>-0.18 (0.46)</td>
</tr>
<tr>
<td><strong>FEV(_1)</strong> /FVC (%)</td>
<td>Intervention</td>
<td>76.7 (7.0)</td>
<td>79.1 (6.7)</td>
<td>2.4 (5.3)</td>
</tr>
<tr>
<td></td>
<td>Comparison</td>
<td>77.6 (10.9)</td>
<td>80.2 (9.5)</td>
<td>2.6 (4.5)</td>
</tr>
<tr>
<td><strong>PEF</strong> (L/min)</td>
<td>Intervention</td>
<td>400 (107)</td>
<td>408 (120)</td>
<td>7 (56)</td>
</tr>
<tr>
<td></td>
<td>Comparison</td>
<td>420 (92)</td>
<td>431 (76)</td>
<td>10 (56)</td>
</tr>
</tbody>
</table>

* Regression model estimate of difference between groups in the mean change in outcome, adjusting for baseline value. \(FEV_1\) = forced expiration in 1 second. FVC = forced vital capacity. PEF = peak expiratory flow.

The importance of focussing on the participants who met acceptability criteria is demonstrated by performing the analysis on all 45 participants’ data (Table 6.38). This shows statistically significant baseline adjusted improvements in both \(FEV_1\) and \(FEV_1\) % predicted scores.
Table 6.38 Lung function results (n=45)

<table>
<thead>
<tr>
<th></th>
<th>Baseline Mean (SD)</th>
<th>Followup Mean (SD)</th>
<th>Change Mean (SD)</th>
<th>Estimated difference* (95%CI), p – value (Intervention – comparison)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FEV₁ (L)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>2.54 (0.57)</td>
<td>2.63 (0.59)</td>
<td>0.09 (0.20)</td>
<td>0.185 (0.027 to 0.343)</td>
</tr>
<tr>
<td>Comparison</td>
<td>2.46 (0.77)</td>
<td>2.37 (0.77)</td>
<td>0.09 (0.30)</td>
<td>0.023</td>
</tr>
<tr>
<td><strong>FEV₁ % predicted</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>83.6 (14.4)</td>
<td>86.5 (13.7)</td>
<td>2.9 (7.0)</td>
<td>6.45 (1.06 to 11.8)</td>
</tr>
<tr>
<td>Comparison</td>
<td>81.0 (14.9)</td>
<td>78.0 (15.6)</td>
<td>-3.08 (16.02)</td>
<td>0.020</td>
</tr>
<tr>
<td><strong>FVC (L)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>3.68 (1.11)</td>
<td>3.53 (0.97)</td>
<td>-0.14 (1.00)</td>
<td>0.163 (-0.252 to 0.578)</td>
</tr>
<tr>
<td>Comparison</td>
<td>3.28 (0.93)</td>
<td>3.11 (0.92)</td>
<td>-0.17 (0.45)</td>
<td>0.432</td>
</tr>
<tr>
<td><strong>FEV₁ /FVC (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>72.0 (13.4)</td>
<td>75.6 (8.2)</td>
<td>3.6 (11.28)</td>
<td>2.1 (-2.3 to 6.4)</td>
</tr>
<tr>
<td>Comparison</td>
<td>75.3 (10.2)</td>
<td>75.3 (10.4)</td>
<td>0.0 (6.44)</td>
<td>0.344</td>
</tr>
<tr>
<td><strong>PEF (L/min)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>388 (99)</td>
<td>400 (106)</td>
<td>12 (56)</td>
<td>3.3 (-31.4 to 38.0)</td>
</tr>
<tr>
<td>Comparison</td>
<td>390 (103)</td>
<td>398 (106)</td>
<td>8 (59)</td>
<td>0.850</td>
</tr>
</tbody>
</table>

* Regression model estimate of difference between groups in the mean change in outcome, adjusting for baseline value. FEV₁ = forced expiration in 1 second. FVC = forced vital capacity. PEF = peak expiratory flow.

6.6.6 Fractional exhaled nitric oxide (FeNO) results

FeNO scores were not normally distributed unless both v1 and v2 scores were logged, and I present both original and logged results (Table 6.39) and neither demonstrate a difference.

Table 6.39 Fractional exhaled Nitric oxide results

<table>
<thead>
<tr>
<th></th>
<th>Baseline Mean (SD)</th>
<th>Followup Mean (SD)</th>
<th>Change Mean (SD)</th>
<th>Estimated difference* (95%CI), p – value (Intervention – comparison)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FeNO (ppb)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>37.5 (34.3)</td>
<td>33.8 (32.0)</td>
<td>-3.8 (27.1)</td>
<td>5.5 (-5.8 to 16.8)</td>
</tr>
<tr>
<td>Comparison</td>
<td>29.5 (24.1)</td>
<td>22.9 (21.4)</td>
<td>-6.6 (13.8)</td>
<td>0.333</td>
</tr>
<tr>
<td><strong>logFeNO</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>3.33 (0.76)</td>
<td>3.17 (0.83)</td>
<td>-0.16 (0.49)</td>
<td>0.14 (-0.17 to 0.46)</td>
</tr>
<tr>
<td>Comparison</td>
<td>3.06 (0.85)</td>
<td>2.87 (0.71)</td>
<td>-0.19 (0.44)</td>
<td>0.361</td>
</tr>
</tbody>
</table>

* Regression model estimate of difference between groups in the mean change in outcome, adjusting for baseline value. FeNO = fractional exhaled nitric oxide. Ppb = parts per billion.
6.6.7 Changes to regular treatments

The results of these outcomes were not normally distributed, and log transformation did not improve this. Therefore the results are presented as median and IQR, with the difference between the groups being assessed using Wilcoxon Rank Sum test.

As described in baseline characteristics the intervention group appeared to use more puffs of reliever inhaler, and less inhaled corticosteroids (ICS) than the comparison group at baseline. There is a statistically significant difference between the change in reliever use at follow-up in the intervention group compared to comparison group (p = 0.022), with the intervention group using significantly less than they started with (desirable) as shown in Table 6.40. However, in the context of much higher use to start with, it is unclear if this is a true difference between the groups, or represents regression to the mean. With regards to percentage of prescribed ICS taken, and equivalent beclometasone dose there was very little change.

<table>
<thead>
<tr>
<th>Puffs reliever per average week</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
</tr>
<tr>
<td><strong>Median (IQR)</strong></td>
</tr>
<tr>
<td>Intervention</td>
</tr>
<tr>
<td>Comparison</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Percentage prescribed ICS reportedly taken</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
</tr>
<tr>
<td><strong>Median (IQR)</strong></td>
</tr>
<tr>
<td>Intervention</td>
</tr>
<tr>
<td>Comparison</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Equivalent Beclometasone Doses prescribed (mcg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
</tr>
<tr>
<td><strong>Median (IQR)</strong></td>
</tr>
<tr>
<td>Intervention</td>
</tr>
<tr>
<td>Comparison</td>
</tr>
</tbody>
</table>

* Wilcoxon on change in scores (v2 – v1)  ICS = inhaled corticosteroids

I collected data about whether participants changed their step on the BTS ladder. Given that to be in the trial participants had to have uncontrolled asthma it was surprising that 3 participants were stepped down. This trial coincided with a locally enhanced service for GPs where they were incentivised
to reduce the number of people on high dose inhaled steroids. From one participant actively mentioning this at a visit, I am aware that this drove the stepping down in that occasion. Otherwise 91% of participants remained on the same step.

Table 6.41 Change in BTS treatment step by follow up

<table>
<thead>
<tr>
<th></th>
<th>Comparison (n = 25)</th>
<th>Intervention (n = 20)</th>
<th>p – value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step down</td>
<td>1 (4.0)</td>
<td>2 (10)</td>
<td>0.768</td>
</tr>
<tr>
<td>No change</td>
<td>23 (92)</td>
<td>18 (90)</td>
<td></td>
</tr>
<tr>
<td>Step up</td>
<td>1 (4)</td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>

* Fisher’s Exact Test. BTS = British Thoracic Society

Figure 6.7 Change in BTS step between groups

6.6.8 Oral prednisolone use and health service contacts

In total there were 4 courses of prednisolone prescribed: 3 in the comparison group (to 3 different participants) and 1 in the intervention group (p = 0.617). The numbers of health service contacts were generally low. There were no hospital or A&E visits for asthma in either group. Six participants from the comparison group visited their GP or practice nurses for non-routine asthma care.
a total of 10 times, and 3 from the intervention group each visited their GP or practice nurse once (p = 0.710). Eight participants from the comparison group attended for a routine review during the study period compared to 5 in the intervention group (p = 0.616).

Table 6.42 Prednisolone courses and health service contacts for asthma over the study period

<table>
<thead>
<tr>
<th></th>
<th>Comparison (n = 25)</th>
<th>Intervention (n = 20)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prednisolone courses</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total courses</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>N (%) with at least one</td>
<td>3 (12)</td>
<td>1 (5)</td>
<td>0.617</td>
</tr>
<tr>
<td><strong>Hospital/ED visits</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total visits</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Non-routine GP/nurse visits</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Visits</td>
<td>10</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>N (%) with at least one</td>
<td>6 (24)</td>
<td>3 (15)</td>
<td>0.710</td>
</tr>
<tr>
<td><strong>Routine GP/nurse visits</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total routine reviews</td>
<td>8</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>N (%) with at least one</td>
<td>8 (32)</td>
<td>5 (25)</td>
<td>0.745</td>
</tr>
</tbody>
</table>

* Fishers exact test

6.6.9 Serious Adverse Events (SAEs), and evidence of harm

There were no serious adverse events recorded during the study period. There was no evidence of harm from using the intervention, there was no significant difference in health service contacts, or courses of oral prednisolone prescribed (suggesting a severe exacerbation).

6.7 Sample size calculations

Our primary outcomes included ACQ and AQLQ, and this allows me to estimate sample size for any future full scale RCT to show a clinically relevant difference. Both the ACQ and AQLQ have a widely accepted minimal important difference (MID) of 0.5 [176]. In the first section I use the ACQ results to inform the calculations.

There are two ways to calculate a sample size, the first is to use only follow up data, and the second is to take into account the correlation between follow up
scores with baseline scores. Once a sample size has been calculated attrition rates should then be taken into account.

6.7.1 Sample size calculation using follow up data only

The calculation used is: \[ N = 2 \times f(\alpha, \beta) \times \sigma^2 / d^2 \]

The explanations are shown in Table 6.43.

<table>
<thead>
<tr>
<th>Shorthand</th>
<th>Explanation</th>
<th>RAISIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N)</td>
<td>sample size per group</td>
<td>to be established</td>
</tr>
<tr>
<td>(\alpha)</td>
<td>significance level</td>
<td>0.05</td>
</tr>
<tr>
<td>(\beta)</td>
<td>1 – power</td>
<td>0.1</td>
</tr>
<tr>
<td>(\sigma)</td>
<td>standard deviation</td>
<td>1.0</td>
</tr>
<tr>
<td>(d)</td>
<td>minimal important difference</td>
<td>0.5</td>
</tr>
<tr>
<td>(f(\alpha, \beta))</td>
<td>([\Phi^{-1}(\alpha/2) + \Phi^{-1}(\beta)]^2) *</td>
<td>10.5</td>
</tr>
</tbody>
</table>

* where \(\Phi^{-1}\) is the inverse of the cumulative Normal distribution function and can be calculated by SPSS

Therefore:

\[ N = 2 \times 10.5 \times (1/0.25) = 84 \]

Per group the sample size would be 84, total sample size required 168.

6.7.2 Sample size calculation adjusted for baseline scores

I used the correlation (0.46) between the ACQ scores at visit 1 and visit 2 to adjust my estimated sample size, using the following calculation:

\[ N_2 = (1 - \rho^2)N \]

Where \(\rho\) is correlation and \(N\) is the original sample size. Therefore:

\[ N_2 = (1 - 0.21) \times 84 = 67 \text{ per group} \ (134 \text{ in total}) \]

6.7.3 Sample size calculation including attrition rates

The attrition rate in the intervention group in the pilot RCT was 20%, therefore it seems prudent to adjust our sample size to allow for this same level of
attrition. Working on the assumption that any future RCT would have the same study length we could use the lower estimate of 67 per group and dividing by 0.8 would give us overall sample size per group of 84, or total 168. Alternatively, I could use the overall attrition rate of 12%, this would reduce the sample size calculation down to \(67 \div 0.88 = 77\) per group (154 in total).

However should the study period in the future RCT be longer than the 12 weeks it was in this pilot, then the correlation between visit 2 results and visit 1 results is likely to be smaller, and there is an argument that sample size should be based on visit 2 scores only. Therefore, taking into account attrition of 20% this would result in \(84 \div 0.8 = 105\), or total sample size 210. However if I used the overall attrition rate of 12%, this would reduce the sample size required to \(84 \div 0.88 = 96\) per group (192 in total).

6.7.4 Sample size using mini-AQLQ results

Mini-AQLQ is a frequently used primary outcome for self-management asthma studies. Table 6.44 shows the above results using ACQ summarised and also provides the equivalent calculations based on using my mini-AQLQ scores. Depending on which outcome is used, whether correlation between visits is included, and which attrition rate is chosen the estimated sample size varies from 130 to 304.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Baseline adjusted</th>
<th>Sample size</th>
<th>12% Attrition</th>
<th>20% attrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACQ</td>
<td>×</td>
<td>168</td>
<td>192</td>
<td>210</td>
</tr>
<tr>
<td>ACQ</td>
<td>✓</td>
<td>134</td>
<td>154</td>
<td>168</td>
</tr>
<tr>
<td>Mini-AQLQ</td>
<td>×</td>
<td>242</td>
<td>276</td>
<td>304</td>
</tr>
<tr>
<td>Mini-AQLQ</td>
<td>✓</td>
<td>114</td>
<td>130</td>
<td>144</td>
</tr>
</tbody>
</table>

\(^*\) ACQ = asthma control questionnaire. AQLQ = asthma quality of life questionnaire

6.8 Discussion

6.8.1 Chapter overview & summary

In this section, I will first summarise the findings in relation to the research questions. I will then describe the strengths and weaknesses of this evaluation,
and the implications for the design of a future RCT, finally providing an overall summary of my conclusions.

This pilot evaluation of the Living well with Asthma website demonstrates that progression to a full scale RCT is feasible and merited. Recruitment targets were achieved, and attrition rates were comparable to rates of other published digital interventions [8]. Unlike similar asthma studies, we had no upper age limit. This is important as our recent metareview only found one study that included participants over 50 years of age, and descriptions of participants’ characteristics were limited [8]. Such information is important to understand the ‘reach’ of the intervention and its’ likely wider applicability. Unusually, we also described the deprivation spread of our participants, and recruited participants from both deprived and affluent areas.

### 6.8.2 Primary research questions

Our primary research questions focussed on recruitment, retention and website use and usability. We also included two clinical measures (ACQ and mini-AQLQ) as it is likely that one of these would be a primary outcome in any future full scale RCT.

#### 6.8.2.1 Recruitment

Despite poorer than projected responses to recruitment, I exceeded our minimum target for randomisation of 50 by 1. Our recruitment was more challenging than expected in two main ways. Firstly in terms of fewer positive responses to our patient mailings than predicted. This lower response rate had several implications: firstly, in terms of workload and cost where we had to invite twice as many people as anticipated (~ £1 per invite) and secondly that we had to recruit twice as many GP practices as we had anticipated.

I responded to the poorer than expected positive response in several ways. Mainly I revised our search strategy to be more targeted to those experiencing symptoms. I also tried a second (more targeted mailing) from one practice, and follow up telephone calls from another. In the first instance the second mailing was more successful than the initial (1.5% randomised versus 0.2% with first): however understanding why that happened is difficult. The first mailing went
out at the start of December (a busy time for people), a printing anomaly meant flat numbers were missing from some addresses, and we were using our original wider search strategy. The second mailing was more targeted (200 invites posted compared to 493), was undertaken at the start of February (arguably a better time of year) and we had resolved the issue with the addresses. Therefore, it is difficult to know how much each of these different issues contributed to the improved randomisation rate.

The latter strategy of follow up phone calls was overall not considered good use of time in this study. As a significant time had passed between the mailing and phone calls there was considerable work involved in crosschecking lists to ensure we did not invite anyone who had already advised us they had declined to participate, and further time was required from the GP to review the list again, in case anything had changed. Although we had anticipated we might use follow up telephone calls or second mailings (and had ethical approval in place), we had not fully incorporated their use into our recruitment systems and therefore implementing them generated considerable workload for the reason above, and also because our search strategy changed during the recruitment. When I did speak to people on the phone it seemed they had heard of the study and simply were not interested, and it is important to state that none of the patients I spoke to appeared annoyed about receiving the phone call.

Follow up phone calls was a strategy found to be useful in a Cochrane review of recruitment methods [199]. For this reason, and because they had worked well on a previous study, [171], I had been keen to include the option of telephone calls. However, there was one important difference: participants in that study could expect to receive approximately £120 over the course of the study, and most people I spoke to on the phone had not got that far in the information leaflet they had received. So when it came up in discussion this new information was of interest. I did not offer any financial recompense for the RAISIN study and in retrospect I feel it would have been fairer to provide a small voucher (£10-20) to recompense people for their time, and may have aided recruitment slightly.

Careful planning of how this additional method would be integrated into recruitment processes in the future would be key for it to be truly helpful. The
main facilitator would be obtaining REC and GP practice approval for removing a password protected excel chart of the patient mailing details and phone numbers - something we did not have with this study. This would allow for researchers to undertake a second mailing or follow up phone calls without having to revisit the practice. If a significant time had passed the updated mailing list (minus those who had already responded) could be sent back to the practice using secure email (e.g. nhs.net), for the GP to review again.

As well as this poorer than expected positive response to the mailing, only 1/3 passed the initial telephone screening, and even fewer actually went on to be randomised. This telephone screening was a considerable amount of work for me and my colleague. A solution to this would be to send out the ACQ in the initial mailing to potential participants, allowing these 75% of patients to be quickly excluded. Self-administered results are as reliable as supervised for ACQ and mini-AQLQ [200], and there is precedence in the literature for this approach [82]. This would markedly streamline the process following receipt of a positive response.

Investigating how the internet could facilitate recruitment would be worthwhile and there are two specific areas it could streamline processes. Firstly to find potential participants in the first place, for example using social media, both snowballing via researcher pages, and also relevant disease specific social media pages e.g. Asthma UK, and this has worked well in a recent cancer study [201]. Secondly it could also be used to streamline the screening process so for those participants who are interested they could be directed to a website which asked initial screening questions including the ACQ for example and then only those meeting initial criteria are called back by the research team.

It is worth pointing out that none of the difficulties we experienced with recruitment related to the workload implications on health professionals suggesting that using NPT to optimise our trial design [111] had been useful. While we had to recruit twice as many GP practices as planned this was not major barrier to progressing with recruitment, I speculate because the workload implications for them participating were minor.
6.8.2.2 Retention

Although challenging, recruitment targets were achieved, and retention rates were comparable to rates of other published digital interventions [8].

However, the difference in attrition between the intervention group (20%) and the control group (4%) was unexpected. My colleague who was managing the trial at this point found that with the 5 individuals in the intervention group a first contact was made, but the participants stated they had not used the website and assumed a follow up visit was not required. When it was explained that a follow up was still helpful these individuals were unable to commit to a date, and then subsequently did not respond to 2 further contact attempts. I speculate that guilt about not using the website contributed to them feeling unable to complete the study. In a future study, individuals could be counselled at the baseline visit in order to reduce this.

6.8.2.3 Website use

The figure of 76% of individuals logging in is comparable with other behaviour change websites [42, 166]. There is no ‘minimum dose’ of exposure to a website that suggests it is more likely be efficacious, and given that the entire website could be navigated in approximately 45 minutes, a mean log in time of 23 minutes seems reasonable, particularly given that some statistical benefits were shown in our analysis.

6.8.2.4 ACQ and mini AQLQ

We included 2 clinical outcomes in our primary research questions - changes in ACQ and mini-AQLQ. Our results indicate a trend towards improvement in ACQ scores in the intervention group which is very promising given this is a pilot study not powered to show a difference. The other outcome we would consider for the primary outcome in a full scale RCT would be asthma specific quality of life (mini AQLQ). We showed a significant improvement in one domain of the mini AQLQ (activity limitation) and approached significance with another (symptoms). The baseline mini-AQLQ score overall was 4.8 (SD 1.0) and is markedly below the cut off for what is considered to be impaired QOL (<5.5) [82], and lower than similar populations described elsewhere in the literature [202].
From the literature there is no single obvious choice for a primary outcome in evaluations of asthma interventions, with one recent workshop (funded by the National Institute for Health Research, NIHR) identifying 11 separate ‘core asthma outcomes’ [135]. My metareview in chapter 4, describes results for 11 different outcome areas (with many more individual measures used). Recently published protocols which I described in the next chapter (7) have asthma control and mini AQLQ as primary outcomes [203], numbers who have obtained/updated written action plan [204], or adherence to ICS [205]. The mini-AQLQ as used in our study does have one limitation in that the environmental stimuli domain has variable relevance depending on where an individual lives, and potentially less likelihood to demonstrate change. For example, questions about cigarette smoke in the environment may be less of an issue since the smoking ban came into force in the UK in 2007, although passive smoking in households is still likely to be an important factor. Questions about pollution may only be relevant to those who live in the areas troubled most by it (e.g. south east of England, and those in large cities such as Glasgow where this trial was undertaken). Interestingly the working group formed by the NIHR to provide guidance did not find any of the available QOL measures met their recommendations, feeling that the AQLQ (including mini version) could be a supplemental outcome only [135]. There are practical considerations too for example the 6 question version of the ACQ (no lung function measure) has only 6 questions, whereas even the mini version of the AQLQ has 15, and the full version has 32.

6.8.3 Secondary research questions

My secondary research questions covered 14 individual outcomes (EQ5D, MMAS, PAM, spirometry, FeNO, medication changes (BTS step, puffs reliever, ICS daily dose, ICS percent prescribed taken), and health service contacts (primary care scheduled, primary care unscheduled, admissions/A&E visits, exacerbations) and adverse events). This range was included to facilitate choosing appropriate outcomes for the future RCT.

The results from the majority of outcomes favoured the intervention with several achieving statistical significance (mini-AQLQ activity limitation domain, PAM activation score, % of participants achieving MID for MMAS, and number of...
reliever puffs taken). There were 3 outcomes where the baseline adjusted between group differences favoured the comparison group and this was the FeNO, FVC/FEV₁ ratio, and PEF. In these 3 outcomes the effect sizes were very small and the confidence intervals wide. There were 3 outcomes which showed completely no difference in either group at follow up e.g. both intervention and comparison group median differences was 0: EQ-5D health utility, % prescribed ICS taken, and daily ICS dose.

That only 22/45 of the participants who completed the study had both baseline and followup results meeting ATS/ERS was disappointing. Therefore I have not proven the feasibility of a researcher undertaking spirometry in the participants own home, a difficulty that has been reported in other studies [206]. Potential solutions include: more intensive training of research staff; use of a device providing test by test acceptability information (cost prohibited me in this respect in this study); or undertaking trial visits in a dedicated clinical research facility by staff experienced in spirometry. However, this latter solution could have a negative effect on recruitment, as 20 out of 96 (21%) of our study visits were undertaken in the evening and weekend, which would not be possible in a clinical research facility. This flexibility around visit times and locations facilitated recruitment of participants who can rarely make it into such RCTs, such as those in full time employment. Even with the option of evening and weekend visits I had 10 potential participants who passed the original telephone screening, but due to difficulties around finding a time to do the trial visit, they changed their mind about participating. Therefore, there is a balance between precision of measurements versus encouraging a more representative sample, and facilitating recruitment. Whether spirometry is required at all in a study aimed at people with mild to moderate asthma is not clear, and there is precedence in the literature for not including these outcome measures in similar primary care based trials, or for using simpler to perform lung function measures such as PEFR [77, 186].

Significant results around adherence and reliever use should be interpreted with caution given the intervention group had poorer levels at baseline, as they could represent regression to the mean. The chance of similar differences in the baseline characteristics would be less likely with the larger sample size required in a full scale RCT. We did demonstrate a significant improvement in the
patient activation measure (PAM), which indicates that those in the intervention group had improved knowledge, confidence and skills to manage their asthma. However there were some issues around the PAM license which would not allow them to provide us with the ‘key’ for translating raw scores into activation scores, instead providing us with a spreadsheet that required individual question scores to be inputted (copy and pasting worked). However the column for the participant number could not be added immediately beside the response columns leaving room for error. This process was feasible for a sample size of 51, I would suggest that if this outcome was going to be used in the future negotiating access to the conversion table to allow this to be done automatically within the statistical software would be essential.

An important finding is that there was no evidence of harm, or serious adverse events related to this intervention, which is important to note as this outcome is rarely reported [8]. No outcomes significantly favoured the comparison group.

6.8.4 Strengths and limitations

Within the confines of a small research team I attempted to reduce bias where possible. Randomisation occurred after baseline data collection, and was handled by a third party automated system. Data management was undertaken by an established clinical trials unit with vast experience of conducting RCTs (Robertson Centre for Biostatistics). All results were reviewed by an experienced RCT statistician (AM or CH). As the researcher undertaking analysis it was unfortunately not possible for me to be blinded to the group allocation as I had preceding knowledge of the recruitment numbers and differences in comparison group (n = 26) and intervention group (n = 25). In a future large scale RCT both the analysis and assessors could be kept blind to allocation.

Although the majority of the spirometry did not meet ATS standards there was no evidence of difference in the standard between the groups, and this issue has previously been well documented in the literature. Removal of the spirometry component of the ACQ to convert it into the 6 question version (a well validated questionnaire in its own right) [198] reduced the effect size only slightly down to -0.36 (-0.96 to 0.23), suggesting that any concerns that substandard spirometry could be significantly impacting on the overall ACQ score was not borne out.
As with many digital intervention the ‘reach’ of the intervention is a potential issue. In the literature review, I have described how many interventions so far have excluded older age groups or not provided details of education attainment or socioeconomic status of participants. However my awareness of this as a potential issue is a strength, and I took extra steps to ensure the later information was available, and in particular to examine whether those from more deprived areas were being screened out (they weren’t), and also we had no upper age limit. This led to our oldest participant being 78. While there are few older participants in digital trials, there are studies of individualised education programmes having positive effects in this age group [207] and it seems reasonable to speculate that as the current internet aware population grows older that any positive effects seen using digital interventions will continue to be effective as people do get older. Only one of digital asthma self-management RCT provided this data [94] who reported that out of the 931 individuals they invited, there were no difference between the 200 randomised and the remainder who weren’t in terms of socioeconomic status (5% living in an under privileged area in participants vs 7.1% not randomised). In this study we know that those who were excluded due to not having access to the internet were older than those who were excluded for other reasons, but there is acceptance that this is less of an issue with year on year increases in the number of households with access to the internet (84% in 2014, Office of National Statistics). What is missing from this picture is the characteristics (age, gender, SIMD) of the 5383 invited overall which would give us a true picture of the reach. It is impossible to collect this data accurately retrospectively, but for future studies, with appropriate ethics committee approvals this could be easily collected.

The poor response rate is a concern, and does suggest that our reach, via GP mailings, may be limited. However as discussed previously in chapter 5, both the literature and user testing suggested that an important route for motivating patients to accessing the website would be via practice nurses at asthma reviews, a strategy that would be worth evaluating in a future RCT. However, given that the average attendance at asthma reviews in Scotland 2013/14 was 78%, this should not be the only method of directing patients to such a resource.
6.8.5 Conclusion

This pilot evaluation shows that the Living Well with Asthma intervention merits further evaluation in a full scale, phase III clinical trial, and that it is indeed feasible to do so. More streamlined recruitment methods, possibly including newer online methods, and further consideration to the requirements for lung function as an outcome are the main areas requiring work prior to moving to a full scale RCT, discussed further in the final chapter. In order to reduce the ‘practical barriers’ to using the intervention the provision of an app to work alongside the website is would be worthwhile to explore, along with consideration of making it modular in nature.

The next chapter formally compares this intervention with recently published comparable studies.
Chapter 7: Comparison with Recent RCTs of Digital Asthma Self-management Interventions

7.1 Introduction

In order to be able to compare the results of my evaluation with comparable studies in the literature I specifically undertook a search of the published literature focussing only on RCTs (including protocols) which were evaluating interventions similar to the one developed here i.e. standalone, digital interactive interventions aimed at adults with asthma. I chose to look directly for RCTs, rather than simply update the earlier systematic review (Chapter 4) for three reasons. Firstly, to allow me to include any RCTs very recently published which would not have had time to feature in any systematic reviews. Secondly, to allow me to examine the primary literature directly and increase my ability to derive directly useful information from them. Finally, I anticipated this literature search would identify protocol papers or abstracts that would provide insights into where this field of research was heading in the future.

7.2 Methods

The PICOS criteria (participants, intervention, comparison, outcomes and study type) I used are similar to that used for the systematic review (see SR protocol, appendix 4) with the main difference being that I focussed on those comparing digital interventions to usual care only, participants with mild to moderate asthma, and studies within the last 10 years. This was to focus on interventions which were broadly similar to Living Well with Asthma. These PICOS criteria are summarised below.

<table>
<thead>
<tr>
<th>PICOS criteria</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>adults aged 16 or over with mild to moderate asthma</td>
</tr>
<tr>
<td>Intervention</td>
<td>digital intervention to promote self-management. Must be interactive, and be used at least in some way independently of health professional</td>
</tr>
<tr>
<td>Comparison</td>
<td>usual care only</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Asthma related outcomes as described fully in the systematic review protocol (appendix 4)</td>
</tr>
<tr>
<td>Study type</td>
<td>Randomised Controlled trial</td>
</tr>
</tbody>
</table>

Table 7.1 PICOS summary of search for included RCTs
I already had a list of RCTs from my own previous metareview [8], which included 4 RCTS aimed at adults [94, 208-210]. In addition a primary systematic review of this topic was nearing completion in my department, and I had a list of the 5 interventions included here, two of which were included from my metareview and three new articles [211-213]. I therefore refined my search strategy iteratively until it included all 7 of these interventions as a way of ensuring that my search strategy was wide enough to reasonably expect to find any similar interventions published since the more comprehensive search for the systematic review was run in August 2014. My final search strategy is shown in Table 7.2, and was finally run on the 3rd April 2015.

**Table 7.2 Medline Ovid search ran on 03/04/15**

1. asthma.ti.
2. self care.mp. [mp=ti, ab, ot, nm, hw, kf, px, rx, ui, sh, tn, dm, mf, dv, kw, ac, de, md, sd, so, tx, ct, bt]
3. self-management.ab.
4. randomi* control* trial.mp. [mp=ti, ab, ot, nm, hw, kf, px, rx, ui, sh, tn, dm, mf, dv, kw, ac, de, md, sd, so, tx, ct, bt]
5. self monitoring.mp. [mp=ti, ab, ot, nm, hw, kf, px, rx, ui, sh, tn, dm, mf, dv, kw, ac, de, md, sd, so, tx, ct, bt]
6. (digital or online or web* or internet or computer* or interact* or phone or smartphone or mobile).ab.
7. education.mp. [mp=ti, ab, ot, nm, hw, kf, px, rx, ui, sh, tn, dm, mf, dv, kw, ac, de, md, sd, so, tx, ct, bt]
8. monitoring.mp. [mp=ti, ab, ot, nm, hw, kf, px, rx, ui, an, sh, de, md, sd, tn, dm, mf, dv, kw, ac, ip, vo, pg, jn, pb, yr, ar, bs, bt, cf, dp, ja, so, pu, ib, is, et, tx, ct]
9. 1 and (2 or 3 or 5 or 7 or 8) and 4 and 6
10. 9 not (paed* or ped* or child*).ti.
11. remove duplicates from 10
12. 11
13. limit 12 to yr="2005 -Current"
Chapter 7 RCT update

7.3 Results

After de-duplication there were 95 articles to screen, of these thirteen were of relevance:

Completed RCTs = 6

Published protocols = 5

Conference Proceedings = 2

The six completed RCTs referred to three individual interventions (with main evaluations published between 2005-2010). Two of these Rasmussen et al [209] and van der Meer et al [94]) had featured in the earlier metareview, and one new RCT (Bender et al) [212], which had not been reported within the metareview.

As referred to above I had used seven interventions when refining this search strategy. I did not subsequently include four of them in this review. This is due to two being aimed at those with moderate/severe asthma [211, 213], one where the comparison group did not receive usual care when examining the primary literature [208], and the final one was not independent of health professional input [210]. However, I thought it was appropriate to use them in my search strategy, as they were the type of articles I was otherwise looking to include.

7.3.1 Interventions evaluated within included RCTs

That the most recent RCT was published in 2010 was surprising. The oldest intervention was evaluated in a trial published in 2005 by Rasmussen et al [209], based in Denmark.

The intervention developed and evaluated by the SMASHING study group (Self-Management in Asthma Supported by Hospitals, ICT, Nurses and General Practitioners) was based in the Netherlands. They have published 4 papers in relation to this study: initial results, subgroup analysis, cost–effectiveness and a long term follow up paper (published between 2009-2013) [91, 94, 144, 214],
plus an additional RCT focussing on adolescents and therefore excluded from this review [215], along with their original RCT results paper [209].

The final intervention described by Bender et al was much less intensive and the only entirely standalone intervention [212].

I will refer to these interventions as Rasmussen [209], SMASHING group [91, 94, 144], or Bender, for clarity in the remainder of this chapter.

7.3.1.1 Baseline characteristics

Despite having access to the primary papers the reporting of baseline characteristics was still incomplete (Table 7.3). The Smashing group provided data on deprivation, smoking status, and educational attainment, which was absent from the other two articles. While Bender did not report any of these characteristics, it did report ethnicity.

There were upper age limits for all three studies, the highest again being 65 years. The majority of participants were female, and the average age ranged from 30 years to 41.5 years.
<table>
<thead>
<tr>
<th></th>
<th>Rasmussen et al</th>
<th>SMASHING Study Group</th>
<th>Bender</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Year</strong></td>
<td>2005</td>
<td>2009-11</td>
<td>2010</td>
</tr>
<tr>
<td><strong>Target age range</strong></td>
<td>18-45</td>
<td>18-50</td>
<td>18-65</td>
</tr>
<tr>
<td><strong>Sample size</strong></td>
<td>300 (100 per group)</td>
<td>200 (99 usual care, 101 intervention)</td>
<td>50 (25 per group)</td>
</tr>
<tr>
<td><strong>Attrition</strong></td>
<td>253 (84.6%) completed (similar dropout across groups)</td>
<td>183 (91.5%) completed (92 control, 91 internet)</td>
<td>□</td>
</tr>
<tr>
<td><strong>age (yrs)</strong></td>
<td>30</td>
<td>i = 36</td>
<td>i = 39.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>c = 37</td>
<td>c = 43.5</td>
</tr>
<tr>
<td><strong>% female</strong></td>
<td>69</td>
<td>i = 68</td>
<td>i = 60</td>
</tr>
<tr>
<td></td>
<td></td>
<td>c = 71</td>
<td>c = 68</td>
</tr>
<tr>
<td><strong>Deprivation</strong></td>
<td>□</td>
<td>5% lives in underprivileged area</td>
<td>□</td>
</tr>
<tr>
<td><strong>Current smoking</strong></td>
<td>□</td>
<td>i = 12</td>
<td>□</td>
</tr>
<tr>
<td></td>
<td></td>
<td>c = 14</td>
<td></td>
</tr>
<tr>
<td><strong>Ethnicity, % white</strong></td>
<td>□</td>
<td>□</td>
<td>i = 44</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>c = 40</td>
</tr>
<tr>
<td><strong>Educational attainment, % high</strong></td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

□ no data provided.
7.3.1.2 Use of theory, development processes and piloting work for each intervention.

Reviewing the primary articles allows me to consider the actual interventions in more detail than was possible in the metareview described in chapter 4.

Rasmussen

The Rasmussen intervention was based on a website that had been freely available in Denmark from 2000 [87], until date unknown (literature suggests was taken offline between 2003 and 2005). In May 2003 it had almost 8000 registered uses, with diary use (self-monitoring) never exceeding 4.5% of the registered users at any one time. Key feedback from quantitative surveys and qualitative interviews of users yielded some interesting findings. The website was criticised for being too complicated with too many unnecessary features. The complicated log in system was off putting to users. The researchers found that users did not fill in the monitoring data daily as requested, but often did it in batches so that the automated advice messages were triggered perhaps several days after the symptoms were actually experienced. As discussed above diary use was rarely sustained and individuals preferred to use the site for brief periods at a time often 5-8 minutes. Participants also described generalised concerns about internet access and using computers (such how to log in) that reflected how new the internet was in 2000, and are less relevant today. In their evaluation paper Rasmussen [209] mention a pilot study of 90 individuals with asthma stating that it was found to be user friendly, but provide no further information, citing a presentation at a conference in Sweden as the source of this information. Unfortunately, there is no online abstract.

SMASHING Group

Unlike the preceding intervention, the development process is not discussed beyond stating ‘we developed a guided self-management tool for adult patients with asthma’. It is also surprising that while they undertook qualitative research to inform development of a subsequent internet based tool aimed at adolescent participants [216], and as part of the trial of implementation methods (discussed in section 7.3.2) [217], there is no evidence that such work was done to inform the version trialled here, and there was no mention of pilot work.
Bender
This results paper provided an outline of how the intervention was developed. They developed a draft of the interactive voice response (IVR) script based on the literature, and the benefit-risk model of health behaviour. This assumes that a person's perception of benefits of using preventer inhalers requires to be addressed in order to improve adherence. This transcript was then reviewed by potential end users through four focus groups. Feedback was then used to refine the script until the final draft of it was then ready for a ‘test phase’. During this 50 test calls were undertaken, resulting in some final refinements. No one in the test phase was subsequently included in the RCT. This indicates that the researchers planning this intervention understood the importance of including end users in the design stage, and appreciated the value of adequate testing. In addition, they cite an earlier study with some overlap of authors on a similar 10 week study that used a face to face interaction between a clinician and a patient, rather than an IVR set up as used here. They used that trial to provide power calculations for this study.

7.3.1.3 Intervention description

Rasmussen
This intervention can be summarised as an ‘online interactive self-monitoring tool’. This trial had three groups: internet group (IG), the specialist group (SG), and the control group/GP group (GPG) as described in Table 7.4, and the study period was 6 months.
Table 7.4 Rasmussen intervention by group

<table>
<thead>
<tr>
<th>Participant Intervention</th>
<th>Internet Group (IG)</th>
<th>Specialist Group (SG)</th>
<th>GP Group (control) (GPG)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intense internet based intervention including electronic diary, an action plan for patients which provided advice directly based on data from the online peakflow diary</td>
<td>Received a written action plan with advice to contact their specialist if deterioration beyond a certain level</td>
<td>Told they have asthma and to see their GP, provided with results of baseline assessment (lung function, reversibility, bronchial challenge and skin prick tests)</td>
</tr>
<tr>
<td>Additional education</td>
<td>Instructed in asthma pathophysiology, treatments and trigger avoidance, and action plan education</td>
<td>Instructed in asthma pathophysiology, treatments and trigger avoidance, and action plan education</td>
<td>No additional education</td>
</tr>
</tbody>
</table>

Smashing Group

The intervention group itself received a comprehensive intervention which was a specially designed website which included the ability to monitor symptoms (via the website, or mobile phones), an internet based asthma action plan (AAP), online education, and web communication with a specialised asthma nurse. The users monitored their symptoms daily, and filled out an ACQ weekly, with immediate feedback. Both groups received basic self-management education (information about asthma, inhaler technique, information about monitoring), but after randomisation the comparison group received just usual care. Follow up was at 12 months.

Bender et al intervention

The final intervention described by Bender et al was much less intensive and an entirely standalone intervention [212]. This interactive voice response (IVR) system enquired about asthma symptoms, delivered core educational messages and encouraged refilling preventer scripts. Users received two calls a month, and those who were symptomatic at either of the first calls received a third call. Each call lasted less than 5 minutes, and covered the three main topics: symptoms, encouraging refills, and education. The comparison group received usual care (e.g. no phone calls). The study length was 10 weeks.
7.3.1.4 Recruitment and attrition rates

Interestingly participants for the Rasmussen trial [209] were recruited from a community sample based on symptoms initially, so only 51% were on asthma treatments when enrolled. Other trials (including my own) recruited those with physician diagnosed asthma.

Attrition rates were provided by two of the three interventions featured in Table 7.3, [94, 209]. Rasmussen reported 84.6% completing their study and van deer Meer et al reported 91.5 %, both impressively low attrition rates when compared to non-digital interventions such as those included in a 2002 Cochrane review on asthma self-management [6]. The third, the IVR intervention, suggests that all participants completed both baseline and follow up visits, as they report n=50 at both baseline and follow up.
### Table 7.5 RCTs summary of results of outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Rasmussen et al</th>
<th>SMASHING Study Group</th>
<th>Bender</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td>Questionnaire based interview: IG improved vs SG: OR 2.64, p=0.002</td>
<td>ACQ adjusted difference showed improvement of 0.47 (0.30 to 0.64) in IG, and more achieved, a clinically significant improvement (48% vs 17%); adjusted relative risk 2.87 (1.86 to 5.14). Symptom free days increased in by 10.9%</td>
<td>ACT - NS</td>
</tr>
<tr>
<td></td>
<td>IG improved vs GPG: OR 3.26, p&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>SG vs GP no difference</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Quality of life (AQLQ)</strong></td>
<td>IG improved vs SG: OR 2.21, p=0.03</td>
<td>Adjusted difference showed improvement in IG 0.38 (0.20 to 0.56). More IG patients achieved clinically significant improvement (54% vs 27%); adjusted relative risk 2.00 (1.38 to 3.04).</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>IG improved vs GPG: OR 2.10, p=0.04</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>SG vs GP no difference</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adherence</strong></td>
<td>Significant improvement for all groups, 'good compliance' significantly higher in the IG vs GPG, and SG vs GPG</td>
<td></td>
<td>Must</td>
</tr>
<tr>
<td><strong>Self care behaviours</strong></td>
<td>Reported use of AAP in: IG (88%); SG (66%); and GPG (6%).</td>
<td>Inhaler technique – NS</td>
<td>Must</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Self efficacy/ beliefs</strong></td>
<td></td>
<td>BMQ. Greater upward shift in positive medication beliefs (p=0.007)</td>
<td>Must</td>
</tr>
<tr>
<td><strong>Health service contacts</strong></td>
<td>Acute unscheduled visits – NS</td>
<td>Physician visits – NS</td>
<td>Must</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Exacerbation rates - NS</td>
<td>Must</td>
</tr>
<tr>
<td><strong>ICS dose prescribed</strong></td>
<td>No change in ICS dose (but more IG on the recommended treatment level).</td>
<td>No change in ICS dose</td>
<td>Must</td>
</tr>
<tr>
<td><strong>FEV₁</strong></td>
<td>IG improved vs SG: OR 3.26, p=0.002</td>
<td>FEV₁ adjusted difference showed improvement in intervention group of 0.25L, 95 CI (0.03 to 0.47)</td>
<td>Must</td>
</tr>
<tr>
<td></td>
<td>IG improved vs GPG: OR 4.86, p=&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>SG vs GPG: NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adverse events</strong></td>
<td>Higher in IG for dysphonia and oropharyngeal candidiasis</td>
<td></td>
<td>Must</td>
</tr>
</tbody>
</table>

* measured by device attached to inhaler or change in cannister weight. ACQ = asthma control questionnaire. ACT = asthma control test. AQLQ = asthma quality of life questionnaire. BMQ = beliefs in medication questionnaire. GPG = General Practioner Group. ICS = inhaled corticosteroids. IG = intervention group. NS = no significant difference. OR = odds ratio. SG = specialist group. × = data not provided or outcome not used
Summary of findings from the three interventions

The results are summarised in Table 7.5. All three of these studies had some positive findings. The Rasmussen trial had three arms, and the internet group consistently did better than the GP group (control group), and the specialist group for symptoms, quality of life and lung function, and better than the GP group but not the specialist group for airway responsiveness. Unfortunately, they did not provide any usage data or qualitative research that would contribute to understanding how the intervention is used in practice, and what topics were more valued by their users.

The Smashing group main evaluation showed improvements in ACQ, AQLQ, FEV\textsubscript{1} and symptom free days. There was no difference in inhaler technique, exacerbations, physician visits or inhaled corticosteroid dose.

Bender et al demonstrated improved adherence and self-efficacy with no differences in symptom scores (ACT) or AQLQ.

In general terms this mimics the results of the metareview - some improvement in some outcomes, more detail (particularly qualitative data) required. What can be said is that symptom scores and AQLQ were only improved in the larger more intensive interventions, however the small sample size of Bender may have had more to do with this than the intervention itself, particularly given that a Cochrane review on adherence reported that to have a reasonable chance of demonstrating an improvement in adherence, evaluations should have a minimum of 60 participants per arm [62].

When interventions are complicated and intensive such as those by Rasmussen and the Smashing group, cost-effectiveness is more important to consider. The Smashing group are one of the few research groups in this area that report cost effectiveness [214] concluding that while the intervention was more expensive than usual care ($254 annually), a willingness to pay $50 000 per Quality Adjusted Life Year (QALY) meant that it could be considered as being cost-effective.

However, I think the most interesting finding here is that of the smaller, less intense and most likely cheapest intervention included: Bender’s interactive
voice response (IVR) telephone calls. This simple intervention demonstrated improved adherence, particularly interesting given they were using objective measures of adherence (device attached to inhaler, or canister weight). Of the three interventions, Bender et al [212] seems most ‘implementable’ and it is this intervention which interests me most in terms of future research directions.

7.3.2 Protocols of RCTs yet to be reported

My search also found three protocols of trials yet to be published. First was the protocol for my own RCT which is found in appendix 1 and the results described in Chapter 6 [33].

The oldest protocol paper found by my search was published in 2011. This described the protocol for a pilot RCT testing an intervention called My Asthma Portal (MAP) [203]. This intervention consisted of a web page accessed by participants, which was linked to a limited version of their electronic health record, and a nurse case manager system. The MAP included tailored education and feedback based on monitoring data entered. It incorporated an asthma action plan, and allowed users to set target goals. This protocol paper reported that recruitment had commenced in 2010, and therefore I actively sought any results. A citation search did not yield any results however searching for other publications from the authors yielded a conference abstract from 2011, providing preliminary process evaluation results. They had recruited 35 of their target of 80, and 75% had logged on once, and usage patterns indicated that users visited the interactive sections (about monitoring feedback) more often than the learning centre which provided general asthma information. Again, this is more intensive than the intervention developed within this project.

I also found a protocol which relates to the interventions evaluated by the SMASHING study group published in 2012 [217]. It is not trialling the intervention per se but the implementation of this intervention that has already been shown in clinical studies described above to be effective. This protocol sees three different implementation strategies being trialled in order to understand how best to disseminate this intervention. The three arms are: minimum support to practices, intermediate support, or extensive support. While not directly meeting my PICOS criteria the results of this study which is the first I have found
of its type will be of interest to any type of internet based self-management support, and therefore merits mention here.

### 7.3.3 Abstracts

One final article worth mentioning is an abstract published in 2014 [92] which describes an interesting trial with a large sample size (490 and counting) which is using sensors on reliever medication and asthma control test (ACT) scores to provide personalised feedback, and educational content via the internet (smartphone or computer). The age range of participants to date is 5 to 80 years and they report interim results at 4 months showing less reliever use and higher ACT scores in both the children and adults. A search of other publications by the authors did not yield any related studies, with all but one named author working for a health care provider based in California, USA. The type of ‘passive’ self-monitoring employed in this trial is exciting and seems likely to be where successful self-management interventions which require an element of self-monitoring will be heading in the future.

### 7.4 Conclusion

Overall this updated search for relevant RCTs, including those not yet published, suggests that while intensive interventions with integrated health professional support continue to be developed and evaluated and appear to be effective across certain outcomes, it is not yet clear whether their use will be sustained in the long term. Interventions which are of low intensity like Bender [212], or that minimise the ‘intervention burden’ for participants featured within the abstract by Merchant [92] are an exciting development, and are more in line with what has been developed and described in this thesis.
Chapter 8: Discussion

8.1 Introduction

The overall aim of this study was to explore the potential role of a digital intervention in promoting optimum asthma self-management to adults with asthma. In order to achieve this aim, I have undertaken a metareview, a literature review, developed a website and carried out a pilot/feasibility randomised controlled trial (RCT).

I followed best practice using the MRC Framework on developing and evaluating complex interventions [100], particularly around the use of theory during development [102, 218], including qualitative methods at multiple stages throughout the development [219], and the use of piloting and feasibility work.

In the results chapters (4, 5 and 6) I discussed the findings of those particular stages of the project; in this penultimate chapter I discuss the findings from the project as a whole. I reflect on how well I have answered the research questions and discuss issues arising from my findings, outlining the overall strengths and weaknesses of the project and finally commenting on what this study has added to the literature. In the final chapter (Chapter 9) I suggest directions for future research, implications for practice and policy and provide overall conclusions for this thesis.

8.2 Reflections on individual research questions

8.2.1 Research question 1

What is known about the effects of online tools to promote self-management of asthma and what helps or hinders their utilisation by patients?

Chapters 2 and 4 provide the answer to this question in full. In summary, the research demonstrated that much of the published literature is of poor quality and short on detail. Nevertheless, there is emerging evidence of the potential effectiveness of digital interventions and I concluded that this project would be contributing to a genuine gap in the available research.
The methods chosen initially to answer RQ 1, metareview, did not ultimately answer the question as I anticipated it would. However, this review did indicate that there was a significant gap in the literature particularly surrounding qualitative articles looking at barriers to self-management. I could not have appreciated this without undertaking the review. Therefore, it is only with hindsight that I can say it may have been more helpful to have chosen an alternative method such as a synthesis of qualitative analyses, or a meta-analysis of the primary literature. Work is underway to fill this gap by colleagues at the University of Southampton who are working on a project ‘Barriers to effective self-management of asthma: A systematic review’ which should be available later in 2015. A recent systematic review of implementation studies of self-management support interventions provides further insight into the facilitators and barriers of implementation [112]. This review synthesizes digital and non-digital interventions so would not have been included in my metareview but the findings are pertinent. In this review, Pinnock et al describe the benefits of a multi-level approach: patient, professional AND organisational [112]. This resonates with what has been described earlier in this thesis, that generally a ‘whole systems approach’ to implementation would be most effective.

Although the metareview did not answer my research question, the results heavily influenced the development, evaluation and reporting of our results. The failings in the current literature identified from the metareview, particularly around sparse use of theory, poor descriptions of participants and a lack of meaningful descriptions of intervention contents motivated me to ensure that this project did not repeat these mistakes. I therefore published a full description of the Living Well with Asthma development and final contents [168] and articulated how we expected it to work.

8.2.2 Research question 2

What are the barriers and facilitators to the uptake and utilisation of a web-based self-management tool from the perspective of adults with asthma, and primary care nurses who undertake asthma reviews?

Focus groups were chosen as the best method to answer this research question, and the full results discussed in chapter 5. Overall, this method worked well, and the findings fed directly into the website contents as planned.
As discussed in chapter 5, the main issue with the focus groups was the particularly wide inclusion/exclusion criteria. While I had a minimum medication requirement (used reliever inhalers a couple of times a month at least) I did not stipulate any maximum medication, or asthma severity criteria. This meant that I had to include participants who were interested in participating even with the most severe of asthma. One participant in the first focus group has such severe asthma she was on continuous subcutaneous salbutamol infusion. While this is a very extreme example, many of the participants had moderate to severe asthma, rather than mild to moderate, and many had experienced multiple hospital admissions. These participants focussed heavily on their personal experiences of hospital care and interactions with medical staff during the focus groups, and it required strong guidance to bring the discussion back to basic practicalities of self-management. Nevertheless, they did provide other more relevant experiences, such as about managing their illness in public, gaps in information, and often demonstrated misunderstanding about asthma that fed into the website, for example with regards to side effects of medications or common concerns and queries. However, in future studies it would be wise to restrict sampling to those who are more closely matched to the intended end users.

One facilitator to increased engagement in adherence interventions is tailoring [60]. Specifically for asthma an example of tailoring is with action plans, which is thought to increase relevance and worth to the individual, and consequently use [64, 71]. Another example is thinking about goal setting where the aim is to agree goals relevant to the individual, rather than the health professional e.g. ‘I want to be able to play football again’ versus ‘I want to maintain my best peak flow’ [78]. Brown et al have shown that good quality user involvement during development can overcome perceived barriers such as socioeconomic status [31], therefore providing different versions of an intervention for more deprived versus less deprived populations seems a logical next step. One area of tailoring which I didn’t explore, and to my knowledge has not been explored in the literature is to consider tailoring of self-management towards different asthma ‘phenotypes’. Asthma phenotypes are recognisable clusters of demographic, clinical, and pathophysiological characteristics [220]. Examples are allergic asthma, late onset asthma, obesity related asthma or neutrophilic asthma [220].
It is already suggested that these different phenotypes have differing pharmacological needs [221], it is a natural progression that these different phenotypes will have different self-management needs, for example obesity related asthma having more focus on physical activity and weight loss, and allergic asthma focussing on adherence to inhaled steroids and trigger avoidance. However, this area of research is still in its infancy, and whether it will become relevant to the field of digital interventions to support self-management is plausible but not yet known.

### 8.2.3 Research question 3

Can evidence from the literature (asthma management and theory) and input from potential end users, be successfully incorporated into an intervention to promote self-management?

How best to connect my findings from the literature and focus groups with the experience of the expert panel eluded me until I was pointed towards Campbell et al’s ‘key tasks’ for intervention development [115]. Agreeing these tasks with the expert panel was a pivotal event for me, and is detailed in full in Chapter 5. During this stage, I gained a feel for what we wanted the intervention to do, and crucially how we expected it to do it. Understanding how we expected it to work clarified exactly what behaviours we were aiming to change, and to what effect. This process is considered crucial for several reasons [102], but most importantly to allow us, as researchers, to understand the results of our evaluations, and work out what has contributed to these results, what worked and what did not work.

Therefore, I need to consider what our results so far tell us about the intervention. What I can say from the data available is limited on two counts. Firstly, this was a pilot study so we cannot comment yet about effectiveness, as it was not powered to tell us this. Secondly, the qualitative analysis of the interviews with the intervention participants is not yet complete, and not part of this thesis. However, within these caveats I can make some comments. As the diagram shown in chapter 5 initially and repeated here (Figure 8.1) demonstrates, the central behaviour we aimed to change was for users of the website to use their medication optimally. E.g. the health professionals
prescribing the best medication for an individual, and the individual making optimum use of that medication.

Figure 8.1 How Living Well with Asthma was anticipated to work

Thinking specifically about this, there was no evidence from this pilot RCT of any difference in attendance at annual reviews or actual prescribing, but as mentioned above it was not powered to show this. However, there was a statistically significant difference in relation to adherence and reliance on reliever inhalers which both favoured the intervention. These results have to be interpreted with caution, given the imbalance between randomised groups at baseline (described in Table 6.4, Chapter 6). Nevertheless, they are consistent with the intervention having the desired effects in a proportion of our participants. As expected the core modules were the most visited, and they focussed on the “recognising symptoms/don’t put up with them” behaviour, promoting ‘best’ medication used optimally. The evidence suggests that a successful strategy for achieving these behaviours is increased use of asthma action plans, and it was an oversight that we did not collect data on action plan use at baseline and follow-up and this would be important for any future study.

I had also hoped that by promoting optimum medication use participants would feel able to increase their physical activity, dedicating a whole section to this. While we did not try and measure changes in actual physical activity, we did collect a related measurement via the mini-AQLQ activity limitation domain.
Interestingly this domain improved by both statistically and clinically significant levels, which given this was a pilot study is very encouraging. Even more encouraging is that out of the eight non-core modules, physical activity had the third highest number of visits, and the second highest amount of time spent on it. Therefore the evidence available is consistent with users visiting these areas of the website, and undertaking at some level the desired behaviours with associated evidence of change in the desired outcomes.

If it seems that this intervention exerts its effects at least in part by increasing physical activity it would be worth considering measuring this in a future full scale trial. This could be done using self-report measures such as the reported metabolic equivalent task (MET)- minutes per week from self-reported walking, vigorous and moderate exercise, or using the international Physical Activity Questionnaire (IPAQ) for example.[222]

As well as using the literature as above to answer the key tasks, I also used it to directly influence the potential components of the website. To my knowledge this was a novel way of incorporating findings from literature and user testing into resource development, and for the purposes of this project worked well, and the answer to the questions is certainly yes, as shown in chapter 5.

8.2.3.1 Reflecting on the items I did not include.

As described in chapter 5, four items had been suggested by either the focus groups or the literature that did not make it into the website, and I discuss two of those in more detail here.

**Standalone friends and family section**

One of these was a dedicated family and friends section, which I, along with the expert panel, felt was not necessary as it would be duplicating contents elsewhere. During the study, I came to regret this decision, from talking to participants at visits and then re-reading the focus group and think aloud transcripts.

It is the one time in this project where we, as the expert panel, decided that ‘we knew best’ and overruled the opinions from the literature and user groups.
Re-reading the focus groups in particular but also the think aloud studies this was identified as a real gap, and the rationale for not doing it was duplication. However, this could as easily have been an argument for just doing it, as it would have been straightforward enough to generate pages based on the rest of the website but changing slightly so they were targeted to friends or family. However, we would have been unable to formally gauge acceptability, without requesting additional ethical approvals to actually test it out on family and friends of those with asthma.

People’s attitudes about managing their asthma, their capacity for undertaking self-management and the level of social support were so intertwined [83] that facilitating support from this source should have been an important component of the website. Such a section could have been a prompt for users to encourage those closest to them finding out more about their illness and how it affects them, and importantly what they could do to help. Given that this would not have been that much extra work, I feel I should have listened better to both the literature and the end users and provided this.

Regular self-monitoring or medication trackers
The literature discussed in chapter 2 suggests regular self-monitoring works, however it also confirms very few people will sustain any level of regular self-monitoring [84, 87]. It was felt that investing time in developing a website component which might work in a trial setting but is unlikely to translate into routine use, was not good use of my time. For self-monitoring to work in real life situations, I believe it needs to be essentially ‘passive’, i.e. occurring without the individual having to do anything. There is some innovative work occurring in this sphere for example using ‘smart inhalers’ which track how often the reliever is used and alerts the user via Bluetooth connections (e.g. to smart phones) that their reliever use has increased and action is required [92]. Overall, I conclude that until a system can be developed where the monitoring requires virtually no input from the users that this aspect of asthma management should not be the focus of attention. Consideration to the workload implications is crucial if self-management interventions are to be successful in the longer term, as we know that increasing treatment burden reduces an individuals capacity to manage other aspects of their lives or reduces
engagement with health care [223, 224]. A systematic review and meta-analysis examining interventions to reduce 30 day readmission rates found that those interventions which worked to support patients capacity for self-care were more effective [225].

However, knowing that self-monitoring can be effective led me to consider what we could do within the website to promote it, in a way acceptable to patients, yet within the confines of my capabilities and the software. It was agreed that the website should promote recognising symptoms in more general terms, including use of the RCP 3 Q [163], the idea being that users would gain some of the benefit of self-monitoring (early warnings of deteriorating symptoms) without having to do the do work when they were well. The salient point being that the burden of interacting with the website had to be less than the mild to moderate symptoms this patient population endured.

Similarly, users in the focus groups had requested a medication tracker to be included, with the particular aim of helping users keep track of how much reliever medication they had used, and when their preventer inhaler would be running out. There are several inhaler brands available more recently which included counters and it may be that this will increasingly be a feature of inhalers in the future. Again, it was felt, probably correctly, that more typical users would not use this feature. Instead, I included a table of typical inhalers and typical usage patterns with how many days a given inhaler should last if it is used X number of puffs a day. For example, preventer inhaler Clenil Modulite has 200 doses per canister so if using 4 puffs a day, users would need to request it every 50 days, and a ‘print this table’ link provided. I believe these were the right decisions for this intervention, particularly given the usage patterns we saw where most people only logged in once or twice over the study period.

8.2.3.2 Is this really a complex intervention?

Throughout this thesis, I have made the assumption that what I developed here ‘Living Well with Asthma’ is indeed a complex intervention. ‘Complex intervention’ has become a bit of a buzzword and the literature on this area has “grown exponentially as rapidly expanding problems in health and health inequities have demanded immediate, inventive and effective solutions.” pg 308
The MRC define complex interventions as: “interventions with several interacting components”. They further recognise that there are several dimensions of complexity, and that complexity is not necessarily limited to the number of components within the intervention package itself, but can relate to outcomes, variability in the target population, number and/or difficulty of the behaviours required by those delivering or receiving the intervention. On one hand, it could be argued that asking people to log on and click through a website is not a complex task, and where are the interacting components? However, I would argue that, as described in chapter 5, the website was asking participants to undertake multiple behaviours, many of which were complicated such as signing up to the ‘4 weeks challenge’, and promoted behaviours such as interaction with health professionals and for this reason ‘Living well with Asthma’ merits being called a complex intervention.

8.2.4 Research question 4

What would be the feasibility of undertaking a randomised controlled trial of Living Well with Asthma, and how would such a website be used by adults with asthma. What would be the effect on symptom score and quality of life measures?

Chapter 6 demonstrates that undertaking this evaluation was feasible, and as planned provides estimation of effect sizes. The complexity involved in evaluating a complex intervention is often under recognised, and awareness of this led me to give great consideration to our evaluation methods. This ultimately paid off, in that we recruited our target sample, and all received access to the intervention. The process of undertaking this RCT was a steep learning curve, and arguably the stage of this project which lends itself most to debate about whether I did it the best way or not, and what would be done differently in our future RCT. I am going to discuss this in terms of the PICOS terms to provide structure to this section.

8.2.4.1 Participant considerations

My metareview from chapter 4 had shown me how poorly described participants from digital asthma trials had been in the past. In response to this, I characterised this RAISIN population in as much detail as possible. Unlike these
previous studies, I collected data about age, gender, socioeconomic status (SES) and educational attainment, making this one of the best characterised asthma trial populations to my knowledge. This study includes socioeconomic status, age and gender of those who screen failed. I also recorded comorbidities of those enrolled which is important given that people with asthma have higher levels of co-morbidity than expected [38]. In addition, unlike most published studies, I did not have an upper age limit, and my oldest participant was 78 years of age. Historically an upper age limit of 45-55 years has been used in asthma trials in order to reduce the chances that participants may actually have COPD instead of asthma. I disagree with that argument as it makes generalising to a typical primary care asthma population more difficult, as a proportion of those may well be misdiagnosed. Therefore, we tried to limit our inclusion/exclusion criteria as much as possible, and ensured that we recruited participants from a range of primary care practices which would include participants from across deprivation deciles. In particular, I was pleased to note that there was no difference in the spread of participants across deprivation deciles in those who were randomised versus those who were found to be ineligible. For future studies maintaining a record of the spread of deprivation in those who were invited to participate, versus those who responded, and ultimately those who were randomised, would be of particular interest. This would allow us to understand better the reach of such an intervention.

Our difficulties recruiting are well described in Chapter 6 and it is interesting to see newer more imaginative methods of recruitment being used in more recent protocol papers for example Arguel et al are making use of consumer groups, google, Facebook, twitter and online noticeboards such as Gumtree [204].

8.2.4.2 Intervention considerations

From the usage patterns, and PETS questionnaire results there are two main conclusions which can be drawn. The first is that despite having to be symptomatic to participate in the study, and 95% of users acknowledging within the first few pages of the website that asthma impacted on their lives, 41% still doubted the personal relevance of the website advice to their own situation. From clinical experience and the literature review I was aware that people with asthma frequently underestimate their symptoms, or assign them to another non
asthma related cause [2, 228]. As detailed in chapter 5 one of our key behaviours was therefore to ‘Recognise symptoms, don’t put up with them (aim for no symptoms)’. However, these results suggest that despite my best efforts a proportion of individuals did not take on board that message from the website, and that would be one area where the website would warrant further development. This would likely involve the feedback being more explicit in what their answers mean in terms of their own symptoms and what they should be aiming for, and possibly reinforcing this throughout the website rather than just during the initial core modules.

The second conclusion I draw is that the way the website is presented to users could be improved. As I suggested in the discussion in chapter 6 (RCT) it would be worth only providing the core modules initially and then adding in additional sections each week, in order to increase the chances that users would click into the new section as it was made available to them.

**Intervention fidelity**

There are many reasons for choosing to deliver an intervention digitally: cost, convenience, increased reach, tailoring, or overcoming isolation for users [229]. Another reason may be ease of maintaining intervention fidelity - everyone gets the same intervention. At least they do on the face of it. However unlike public health based interventions which may well work entirely independently from health services (e.g. smoking cessation), interventions such as this to support self-management may be *delivered* independently from health professionals, but they cannot *work* independently from health professionals. For example, one of the core behaviours for Living Well with Asthma was to optimise best medication use. Any change in prescribing relies on an interaction between the user and multiple health professionals (practice receptionist, primary care team and pharmacists). Access to, and quality of, health professional reviews for asthma may vary from practice to practice as indicated by our asthma participants in stage 2. It is well recognised in the literature that many complex interventions fail to achieve any meaningful changes, and those that do in a trial setting are often hard to sustain in real-life settings, or be replicated in different contexts [102, 226] [100]. Hawe [226] argues that historical obsessions with standardising interventions and not allowing contextualisation of interventions has contributed
to many community based interventions showing very small or no effect, and I believe the digitally delivered interventions will not be immune to this.

Arguments for increasing emphasis on standardising the function, rather than the form is gaining momentum [227, 230]: here intervention fidelity is assessed by how well the intended function, rather than form, matches. This fits with Michie et al’s taxonomy which aims to allow researchers to characterise an intervention by its constituent functions (in this case behaviour change techniques (BCTs)), allowing for the form each BCT takes to be contextualised within individual settings.

Another researcher, in another setting, might look at our development processes and the BCTs we include in our intervention, and develop quite a different intervention, particularly with a different set of user testers. This is not wrong, and in fact allowing for the ‘form’ of an intervention to incorporate local contexts is thought likely to increase the chances of effectiveness, where it exists, being demonstrated [230]. There are practical examples of this occurring [226, 231]. Again, the StopAdvisor smoking cessation website is a excellent example of this where it was ‘contextualised’ towards users with lower SES by all user testing being done by participants with low SES, to the degree that it then only worked in this group [31].

8.2.4.3 Comparison group considerations

One area of contention when planning a RCT is what intervention, if any, should a comparison group get. This is more so when the mode of delivery itself is considered part of the intervention, which historically was the case particularly with internet based evaluations. For example in their systematic review Griffith et al [229] berate that most interventions are not compared to a traditional delivery method such as face to face, or classroom, but rather ‘usual care’. They claim that understanding the added benefit of using the Internet to deliver the intervention is of great importance. This may have been the rationale for Ryan et al [186] providing their comparison group with a paper based version of their mobile phone based intervention rather than the mostly likely less intensive ‘usual care’. However, this can lead to a situation, as happened with Ryan et al, where both groups demonstrated an improvement, and therefore
how to proceed is not very clear. We do know that paper based self-management interventions can work in trial settings [6, 65], however we also know that they do not become integrated into every day practice, either by patients or by health professionals [1, 5, 9, 68], questioning the rationale of using it as a comparison group. Therefore, I feel this view is outdated, and potentially negatively impacting progress by diluting the potential effects of new interventions. If the mode of delivery is novel, or of particular interest then at the very least the trial could have a third arm of ‘usual care’. There are examples of this in the literature in other disease areas such as Lorig et al analysis of the Chronic Disease Self-Management Program (CDSMP) which evaluated their Internet version vs small groups (traditional methods) vs usual care [232], and asthma itself by Rasmussen et al [209] which had an internet group, a specialist group and a usual care group.

An alternative way of looking at the evaluation of internet based interventions is to focus the evaluation on the content itself, rather than the delivery method. A recent example of this is where the intervention group received an interactive smoking cessation behaviour change intervention and the control group were provided with a link to a static web page covering standard smoking cessation information [31]. Interestingly this allowed participants to be blinded as to whether they were in the intervention group or not, a feat that often eludes complex intervention evaluators. In this particular intervention evaluation, they randomised over 4000 individuals, so providing a face to face, or paper based alternative would be futile and costly, as it would differ so hugely from the intervention under evaluation. The beauty of a standalone internet based intervention is that it can be delivered (and potentially evaluated) at scale, and control groups should really reflect this.

For future evaluation of Living Well with Asthma, I would particularly like to see two types of evaluation being undertaken in order to truly understand effectiveness, and implementation potential. Firstly, a ‘traditional’ type as undertaken here, but clearly on a larger scale and incorporating changes suggested by our findings, but also a second parallel evaluation undertaken entirely remotely, with no face to face contact. Ideally participants would be identified in the same way they would if this intervention was made freely
available – practice nurses mentioning it during asthma reviews. Those interested in the intervention would attempt to log in to use it, and would be screened and randomised online, and follow-up questionnaires etc. filled out online where available, or via post if required. Users would be randomised to the intervention or a link to either some basic asthma information or Asthma UK website. This could run alongside a more standard trial with typical ‘trial visits’ to allow for lung function and inflammation measures to be taken, as happened here. Other study design considerations are discussed in section 8.2.4.5 below (Study Design Considerations).

8.2.4.4 Outcome considerations

Overall, the majority of the outcomes worked well in this study and as described in the RCT chapter (chapter 6), the main issue was with spirometry. Potential solutions to this issue were described in chapter 6.

At a more fundamental level many of my outcomes were patient reported outcomes and the trend for these has come and gone in the literature, with recent interest particularly in their potential role specifically as quality markers of clinical care [233]. The limitation of surrogate end points as proof of clinically relevant effects is well recognised, and in other disease areas the concentration on surrogate clinical markers has actually led to harm, particularly in diabetes [234]. Therefore, in this study we chose a range of both patient report and objective measures, alongside measuring medication use and health service contacts.

8.2.4.5 Study design considerations

The MRC Framework states that feasibility and piloting are crucial stages when developing complex interventions. As discussed in Chapter 3, and described in Chapter 6, I chose to do both with this evaluation, in order to prepare as much as possible for a future RCT. This could be seen as a risk, as feasibility outcomes could suggest that the intervention would need significant changes, potentially invalidating our pilot findings about recruitment and retention. Given the degree of user involvement and work that went into developing the resource to having the best possible chance of being effective, I deemed this risk was
acceptable, and ultimately the suggested changes to the intervention summarised in section 8.2.4.2 earlier in this chapter are relatively minor and are unlikely to impact on recruitment and retention rates significantly. One drawback to doing a pilot study at this stage was that 26 participants did not provide website use data, despite requiring a significant amount of work on our behalf for recruitment and study visits. Formally providing website access to the comparison group at 12 weeks would have been an option, with a third streamlined data collection point at 24 weeks, where users could have self-administered the questionnaires and posted or emailed them back to me, providing us with limited results and usage statistics on a further 26 individuals.

Another option would have been to have proceeded with an uncontrolled pilot study as seen with an online smoking cessation intervention, also developed using LifeGuide [150]. They argued that including a control arm for an under powered analysis may not be necessary, and for the cost would have added little value in such well-established fields of research such as smoking cessation. Indeed many of the recent systematic reviews of adherence interventions in particular have lamented the number of underpowered studies included [62, 235]. There is an argument that asthma is a similarly well researched field, however the use of online resources in asthma is not as well established as with smoking cessation. My literature review found only one completely standalone intervention with no health professional (HP) involvement at all aimed at adults with asthma, and this was using mobile phones and based in the USA [212]. There were two other interventions which could function without HP intervention but had it as an option and were set in Denmark [209] and Netherlands [94]. Therefore the absence of any UK based comparable interventions suggests that in this situation a control arm was warranted. We reported a non-significant difference in attrition rates between groups, combined with lack of use of the website in this group suggests that non-users in the intervention group may be less likely to comply with follow up, suggesting that this area is not well understood.

8.3 RCT ethical considerations

As with any clinical trial, there were some ethical considerations encountered and these are discussed here.
8.3.1 Collective ethics vs individual ethics

There are two important ethical considerations applicable to all RCTS: collective ethics and individual ethics. Collective ethics refers to the process of assessing new treatments so that future patients will be able to benefit from superior care, i.e. the individuals in the study may not gain any benefits themselves. Individual ethics takes the stance that individuals should receive the best available treatment for their condition.

It is considered important that researchers balance collective ethics with individual ethics when considering clinical trials. Randomisation is considered essential to satisfy collective ethics - otherwise there is a risk patients may be involved in trials which are likely to be biased, leading to conclusions which cannot be relied on, and therefore the patients have been exposed to individual risk without any collective gain [236] (page 455).

In order to satisfy individual ethics potential participants must give their informed consent that they understand the purpose of the study, and their role within it. Traditionally from a researcher point of view clinicians can only enter a patient into a trial if they are genuinely unsure if the intervention is helpful - any clinician who strongly believes one intervention to be better cannot enter a participant into a study - it would be unethical if they genuinely believed they might be exposing a person to an inferior treatment. However, the MRC Framework states “before undertaking a substantial evaluation you should first develop the intervention to the point where it can reasonably be expected to have a worthwhile effect”. Considering these somewhat opposing views left me in a predicament. I had developed an intervention which I genuinely believed to be beneficial to people with asthma, yet I had to be comfortable randomising individuals to the ‘usual care’ group. This very dilemma became an issue during the very first patient visit. During the visit, it appeared clear to me that this lady was suffering asthma symptoms due to not taking her preventer inhalers, due to misconceptions which I was fully aware were challenged within the website, and that if the website worked as I hoped the chances were she would start taking her preventer inhaler regularly and would feel better. In particular, her personal circumstances were very similar to those contained within a vignette in the introduction module, that I was sure would resonate with her.
was taken aback at how strongly I wanted this participant to be randomised to the intervention group, and my disappointment was considerable when our automated system allocated her to the control group. This was real confirmation to me that automated randomisation processes are truly essential to ensure that a researcher’s individual ethics do not interfere with allocation of subjects, which has unfortunately been shown to happen many times in the past.

Later I reflected on this participant, and my own feelings about her allocation, and in particular, I questioned whether I could be the best person to be undertaking these baseline visits, if I felt so strongly that the intervention was beneficial. Was it unethical of me to participate in the randomisation of individuals to a level of care which I believed to be inferior? I strongly felt that the information provided in the intervention was beneficial to participants, however the information provided essentially matched what should be provided in a comprehensive face to face asthma review, which all adults with asthma have access to – including this one. All researchers with an interest in asthma know that people who undertaken guided self-management have better outcomes. With regard to the website, while I felt sure if she used it as I felt it was designed to be used she would have gained some benefit, I could of course not predict whether even if allocated to the website she would use it, whether she would visit the pages I personally thought would be most helpful and whether she would enact any of the behaviours we were promoting even if she did log in and visit every page. Therefore, I realised that while I knew that optimum self-management works, I did not know whether supporting self-management via this website would work, and therefore my concerns around individual ethics could be satisfied.

8.3.2 Missing data

As well as being disappointing from an analysis point of view the missing spirometry data (i.e. the 23 participants whose spirometry tests did not meet acceptability criteria), has ethical implications. In 21 of these 23 cases, the data could not be analysed due to not meeting reproducibility standards. When undertaking trial visits both KS and I were aware that this was occasionally happening, but it wasn’t until I undertook the final analysis that I appreciated how much of a problem this was going to be. This is partly due to the fact that
both visits needed to meet the criteria, so if one didn’t then the other valid measurement didn’t count for anything. Therefore although only 21 out of the 45 (47%) who completed had both v1 and v2 measurements meeting ATS reproducibility criteria, 67 out of 96 (70%) of individual measurements met the criteria.

Spirometry is not an easy investigation for participants to undertake; most don’t like it, find it uncomfortable and tiring, and on several occasions it triggered symptoms that resulted in them requiring to take their reliever inhaler. That 23 individuals went through this procedure for no overall gain to the study is very disappointing. It does however highlight the rationale for a pilot study, as had this been a main evaluation this number would have been much higher.

This issue highlights the importance of either finding a machine that can facilitate meeting acceptability criteria, or considering a different outcome for a future evaluation. It is likely that improved training may have made a slight difference as 63% of the first 30 spirometry tests were acceptable, compared to 77% of the final 30 tests undertaken, but this would not be enough to markedly improve the numbers meeting acceptability criteria.

8.4 Strengths and weaknesses of project

Within each of the main results chapters (4, 5 and 6), I have provided the strengths and weaknesses of each section. This section summarises the strengths and weaknesses of the project as a whole, focussing on overall methodological issues.

8.4.1 Methodology

A key strength of this project is the way that we followed best practice guidance during both the development and evaluation phases. For this, I chose to use the MRC document Developing and Evaluating Complex Interventions: new guidance [100] as the overarching framework to follow, and Figure 8.2 below shows how my methodology maps onto this framework.
Using this guidance resulted in our intervention being theory informed and incorporating user testing, both of which are increasingly seen as essential [100, 102, 219, 237]. I also considered implementation factors from the very beginning by making use of my experience of normalisation process theory [101]. This led me to consider what would happen if I developed an intervention which ultimately was shown to be effective. I made links with Asthma UK recognising that the popularity of their website could be utilised for the benefit of this intervention, and they agreed that they would be open to ultimately hosting and maintaining such a website in the future.

I have latterly become familiar with Penelope Hawe’s work, and in particular her discussions around the merits of evaluations in ‘ideal world’ versus ‘real world’ contexts [226]. Ideal world evaluations are where the interventions are
designed in what researchers consider optimum conditions and are tested in randomised controlled trials, in so called efficacy trials. The alternative approach Hawe proposes is the ‘real world’ approach where understanding effectiveness rather than efficacy is the aim. Ultimately most trials fall somewhere between, and I believe our trial was as real world as possible as evidenced by unrestrictive inclusion/exclusion criteria, and that participants were simply provided with the website address, as they would be if this intervention was ultimately available.

Hawe also discusses a ‘real world’ versus ‘ideal world’ approach to developing interventions. Rather than the more traditional scenario where researchers develop an intervention and then test in the target populations she describes an alternative scenario where ‘community researchers’ identify promising areas of ongoing practice in real life community settings and seek ways to transfer and test these promising practices for wider use in other communities. This resonates in some aspects with the MRC framework approach to developing interventions illustrated in chapter 3 (Figure 3.2) which demonstrates a continuous circular route between developing, feasibility/piloting, evaluation, and implementation, and back to developing again, without specifying which of these 4 individual elements should be the starting point [100]. Hawe calls this approach a ‘bottom up approach’ versus the more traditional ‘top down approach’. I consider that this insight about the potential benefits of the bottom up approach provided by Hawe is not too dissimilar to the argument that implementation scientists have been making for many years: that understanding implementation potential has to start at the earliest stages of intervention development [111], to the point which is argued here by Hawe where implementation is considered first and foremost i.e. what is already seen to be working.

Ultimately, Hawe is not stating one way or the other is necessarily superior, but that whichever camp you are in, you can benefit from considering the alternative view point. In this study by understanding what was actually happening on the ground, both by using my own clinical experience, experience of the expert panel, and specifically looking for gaps in self-management support strategies via focus groups and the literature, then the intervention
contents naturally followed from this. Our aim was never to try and do what was being done better, it was to try and fill the gaps made by the current processes. Therefore what has been developed should work well alongside current practice, supplementing the currently available health professional review, but plugging gaps in the support and information available between reviews.

With further reference to implementability, the content was developed specifically that it would not become ‘out of date’ too quickly, so for example actual knowledge, particularly about specifics of individual inhalers for example was kept to a minimum, with the focus on encouraging the user to think differently about their own asthma.

My flexibility about choice of methods is a strength of this project. I was responsive to my results and where necessary modified methods, for example following the metareview. Similarly, there were occasions where I selected, tried out and sometimes rejected techniques as I felt appropriate, for example when using NPT during the focus group analysis, when it became apparent that the data naturally fell into either barriers and facilitators and further more detailed analysis was unnecessary.

One of the weaknesses of the study is the sampling of the participants in the focus groups, and to a lesser extent, the think aloud studies. These individuals had much more severe asthma than those whom the intervention would be aimed at, as discussed in chapter 5. This latter fact is important to acknowledge as there is increasing evidence that when interventions are co-designed with people similar to your target group they will be more effective in that target group. This is seen with Brown et al smoking cessation [31] which was designed exclusively with smokers with low socioeconomic status. Their results demonstrated that the intervention was only effective in populations with low socioeconomic status, illustrating the power of user testing with the right populations. This was less of an issue with the think aloud studies which were much more focussed on usability issues and there is an argument that these do not even need to be done by those with the disease of interest, so long as someone is clicking through and trying to use the website and providing feedback on their experiences [116].
I was more careful with the inclusion/exclusion criteria for the trial to ensure they matched the target populated defined during the ‘key task’ exercise in chapter 5.

### 8.4.2 Is this truly a mixed methods study?

This study was a mixed methods project, the merits of which are outlined in chapter 3. However, I would like to spend a moment considering just how “mixed methods” it ultimately was. In the first phase we hoped to include qualitative systematic reviews, however as described in chapter 4 I did not find any meeting my inclusion criteria. In the second phase, I undertook focus groups and think aloud studies, both using qualitative methods of gathering data. In both cases, I planned to undertake a framework analysis of transcripts informed by normalisation process theory (NPT) which I had used successfully in this way in past studies. However, in both situations when I received the transcripts and attempted the analysis I found that it simply wasn’t working. With regards to the focus groups, this was for 2 reasons. Firstly, it had been difficult to maintain focus on the topic guide I had developed, and therefore there was a significant amount of data that was irrelevant to the aims of the phase. Secondly, the data that was relevant so obviously fitted into two main areas of barriers and facilitators, that further classification using NPT was not necessary. Qualitative data analysis usually means going beyond simple descriptions, but to transform the data into something new, gaining fresh perspectives on the data. At first look it appears that I did in fact simply describe the data. However, this data was combined with extracts from the literature review, connections made, and new data generated in the form of ‘website features or components’ a process fully described in appendix 10 (intervention planning document). Therefore, although the results are not reported in the style of traditional qualitative results, the data gathering, and analysis, fit within the umbrella term of qualitative methods. With the think aloud transcripts the vast majority of the data was specific to a given sentence on a page, or a page layout. Therefore, the actual data that was analysable from a framework perspective was limited, and naturally fitted into groups entitled ‘content’, ‘layout and navigation’ and ‘user experience’. Comments relating to graphics used were considered somewhat separately, as I was advised that comments about graphics are often personal to participants and not generalizable to others (personal
communication Prof Lucy Yardley). In addition, contrary to epistemological descriptions of qualitative methods I counted the number of responses in each category, particularly interested in whether they were positive or negative. However this is justified as we were looking for specific evidence that those participating in the think aloud studies had felt able to criticise it in front of me, given my role in the developing the website.

This section provides evidence that although the qualitative analysis methods were perhaps not traditional in the sense of employing grounded theory methods, or typical framework analysis, they were chosen in response to the type of data gathered and the requirement of the research question, possibly in part influenced by my positivist leaning stance, but regardless they were right for this study. So while it perhaps was not as ‘mixed method’ as it set out to be, it still is a mixed method study, and in doing so has broadened my own research experience and skill set considerably, and strengthened our findings by providing context and end user opinion.

### 8.5 Summary

This chapter illustrates how the project work has answered my research questions, and reflects on issues raised during the course of the project.

Future research directions and implications for practice and policy are provided in the next chapter, along with my overall conclusion.
Chapter 9: Future Directions & Overall Conclusions

9.1 Introduction

This final chapter discusses future research directions, and considers implications for practice and policy. I then summarise the results and provide overall conclusions.

9.2 Future research directions

9.2.1 Promoting complexity versus intensity

As discussed earlier complexity is not easily defined, never mind measured. It could possibly be defined as the number of behaviour change techniques present, or how many ‘working parts’ there are to it, how long it takes an individual to ‘do’ an intervention, or on how many ‘levels’ it works at e.g. patient, professional or policy. I use the term complexity as a way to describe the interventions itself (including evaluation), and intensity to refer only to the anticipated work that an intervention requires of a user. There is evidence for increased effectiveness in several of these suggested components of ‘complexity’. Powell et al. in their Cochrane review of self-management for asthma found that reducing the ‘intensity’ of the education or level of clinical review may reduce effectiveness [65], however this was based on one single trial of participants with asthma severe enough to require A&E attendance or secondary care referral. The intensive intervention involved a structured theory informed programme, and the basic intervention was simply information delivery about self-management e.g. inhaler technique. Therefore it could be argued they were really evaluating complexity as much as intensity.

With regards specifically to behaviour change techniques the evidence so far suggests that interventions which incorporate more behaviour change techniques tended to have larger effect sizes compared to interventions that incorporated fewer techniques [141, 142]. Pinnock et al. demonstrated that interventions that addressed patient, professional and organisational factors showed the most consistent improvement in outcomes [112]. Overall in the literature there
remains a lack of clarity of the terms complexity and intensity, although the situation is improving.

On the surface the above findings suggest bigger is better, however I would argue that this is not as straightforward as it may at first seem. What is missing from the literature is how does the complexity of an intervention, and its’ intensity impact on sustained engagement by patients - how likely are these complex intense interventions to be implemented, integrated and ultimately embedded in non-trial contexts. The work put in to interacting with any intervention should be balanced ideally with reduced symptom burden, reduced work of monitoring their own illness, and reduced attendance with health professionals, all aspects of patient work which are increasingly being recognised across chronic illnesses, and this work can be considerable [224, 238, 239]. However, in individuals with mild to moderate asthma with a variable disease burden it is difficult to see how the increased work involved in more intensive interventions e.g. those requiring daily self-monitoring for example, would ever be balanced in a population where even those found to be enduring very poorly controlled asthma symptoms, minimise their symptom burden, do not undertake any type of self-monitoring, and often do not attend health professionals for their asthma [2].

From a health services perspective interventions need to demonstrate cost-effectiveness, or at least cost neutrality, for them to be attractive to policy makers and health care providers. This is where standalone internet interventions may find their place. A recent comprehensive review of self-management interventions by Panagioti et al across multiple disease areas found evidence of a consistent, but small, positive effect of self-management interventions (digital and non-digital) mainly in respiratory diseases and cardiovascular diseases [240]. Of most interest to me was the lack of difference in the effect size between less intensive interventions to support self-management, and those more intensive interventions labelled as case-management.

Only 5% of interventions included in this review were ‘pure self-management’ working entirely independently of health professionals. However, with such ‘pure self-management interventions’ once developed, the running costs are
minimal, and even taking into account the costs for contextualisation at local levels, are comparatively easy to disseminate widely, when compared to interventions requiring integrated health professional support. Given the low percentage of stand-alone interventions in Panagioti et al.’s review, this is clearly an under-researched area, further evidencing the need for studies such as this undertaken here.

It seems likely that individuals with mild to moderate asthma are more likely to engage in interventions in the real world which require the least amount of work for them e.g. are less intensive. While there is evidence above that more behaviour change technique and intervention components produce greater effect sizes, generally the evidence suggests these are not well implemented in real life [1, 90]. There is no evidence that more intense interventions are more effective than low intensity interventions in respiratory conditions [240]. This leads me to conclude that research should be focussing on standalone low intensity digital interventions such as this, and that featured in Bender et al [212], as their implementation potential is higher, and running costs likely to be lower. I would conclude that the way forward from here is a website or App that promotes behaviour change tailored to the individual similar to that trialled here, coupled with infrequent automated telephone messages such as those used by Bender [212] or emails, would be a successful combination. Further qualitative work would be required to understand how these changes to this intervention would be received by end users, and potentially work in practice. In addition, further work examining the cost effectiveness of such interventions is merited.

9.2.2 Implications for Living Well with Asthma website development

Previous research on an asthma self-management website indicates that users like to spend 5-8 minutes per session [87]. Our exploration of usage patterns suggests that some users missed sections that they would potentially have benefited from accessing. These two facts combined lead me to conclude that rather than presenting the whole site to the user and not changing it over the course of the study period it would be better to provide the core modules initially and then ‘release’ further sections fortnightly or monthly. This would
encourage the user to return to the site, and complete the new section, a strategy that has been used successfully for a weight loss intervention also developed using LifeGuide software [166].

Our PETS questionnaire results suggest that time and opportunity were the main barriers. It is worth noting that 41% acknowledged there were some barriers in the ‘doubts about efficacy’ subgroup. However looking at the questions that feed into this subgroup they are:

- I skipped the therapy because I was not sure it was helping
- I skipped the therapy because it did not seem relevant to my symptoms and problems
- I did not carry out the therapy because I was not convinced it was right for me

Therefore I think it is truer to say that many individuals in the study felt that it was not relevant to their situation. This links back to the initial problem explored in our planning stages in chapter 5 that showed people with asthma often underestimate their own symptoms and the impact asthma is having on them. These PETS findings suggest to me that future iterations of the website needs to work harder at persuading individuals that they are candidates for enjoying better asthma related health, and the results of the qualitative interviews with intervention group participants may yield strategies for achieving this.

### 9.2.3 Implications for future RCT study design

Extrapolating the results from this study to inform the sample size for a full scale trial is not straightforward. Depending on which outcome is used, whether baseline scores are taken into account, and whether we use the conservative attrition rate of 20%, or the average of 12%, the sample size required varies from 114 up to 304. Whether we take baseline scores into account depends mainly on whether we would change the length of the study period. Given this is a rather simple intervention 3 months seems a reasonable timescale, but it would be wise in any future RCT to include a follow up at 12 months to see if any effects are sustained. The mostly likely design would be using ACQ as the primary outcome,
and given the likely longer study length in a full scale trial baseline adjusted calculations are less valid. Using the higher attrition rate of 20% this results in sample size requirement of 210. I speculate that guilt about not using the intervention contributed to the higher attrition in the intervention group and it is possible that more actively counselling against this at the baseline visit may ameliorate this slightly. It is true that we did say to do this to some extent, but this was balanced against not wanting to seem as though using the website did not matter at all, and I think in a future trial it would be worth being even more explicit about it.

One of the most important areas to learn from our pilot trial is regarding recruitment (including screening). Recruitment methods are highly dependent on choices made around data collection, and for similar face to face data collection methods as used here, we would have a range of options. As discussed earlier making use of internet based strategies would be worth investigating. Using disease specific websites such as Asthma UK would no doubt generate some participants, however they are unlikely to be typical of the participants we are targeting with this intervention (mild to moderate) as I discovered when recruiting for my user design groups (chapter 5). This effect could be reduced by having upper ceilings for ACQ, or certain medications (e.g. those on BTS step 4 or higher could be excluded). Other options would be a link from the NHS information pages, and general snowballing techniques using social media. Other methods worthy of consideration could include local newspapers and bus stop advertising for example. I did consider these for this study but costs seemed prohibitive (£3000-£5000). However in reality I spent in excess of £5000 on mailings alone, and this cost did not include the considerable time spent making up recruitment packs, which could overall be estimated (conservatively) at 1 per minute - over 2 weeks of full time work, which could be avoided if initial contact was made through alternative means.

The other option to consider is whether there needs to be a face to face visit at all for recruitment. It is possible that recruitment, screening, consent, data collection and randomisation could happen online, and users simply allocated website access or not. Follow-up data could also be collected online. It is likely this type of trial would be cheaper to run, however the type and volume of data available to collect would be significantly limited, and it is likely that attrition
rates and missing data would be higher without the impetus of a face to face visit to encourage participants to complete the study. This would need to be taken into account when calculating sample size calculations. This uncertainty about optimum recruitment strategies suggests that further exploratory work on optimising recruitment may be required before this intervention proceeded to a full scale RCT.

When considering recruitment options, one strategy which would significantly facilitate recruitment would be to remove the requirement for participants to be symptomatic from the inclusion criteria. The argument for doing so would be that asthma is characterised by variability and therefore just because a person is well controlled on one day, does not necessarily mean they would still be controlled even the following day. This would more readily reflect real life, when if such a resource was made freely available in the future it would likely be so for anyone with asthma, not just those with symptomatic asthma. If the evaluation was to be over a 12 month period, a potential timescale discussed earlier, removing a baseline symptom score criteria makes more sense. This would have implications on choice of outcome measures. It might suggest a move away from symptom score measure such as ACQ, unless there was scope for serial measures to allow for the analysis to take account of natural variation in scores. Alternatives for the primary outcome could be asthma related quality of life measures which is commonly used as a primary outcome in asthma trials, or even patient activation measure, as a way to quantify if the resource has been successful for the individual.

As well as consideration to recruitment strategies, further investigation of how this intervention might be presented to potential users, should efficacy be demonstrated, is warranted. In the trial setting 76% of those who were allocated to the intervention group logged in, which for this type of study is comparable to that seen in similar interventions. [42, 166] What is not clear is how to best to translate this trial finding into everyday clinical settings. Participants in the focus groups and think aloud studies reported that the intervention being promoted by a health professional would have an important role in their decision to use it. Further feasibility work with health professionals to explore this aspect would be essential before any further full scale evaluation, particularly as this could lead to new findings about potential recruitment strategies for such
trial. There are still the findings from the qualitative interviews with intervention group participants to assimilate which may give some indications towards these issues.

As alluded to above most of the outcomes worked well. The main concern regarding choice of outcomes is around feasibility of undertaking spirometry in this setting. Potential solutions are described in chapter 6 and careful consideration to including this outcome is required, as would be including the PAM with regards to the practical concerns about the ability to undertake the analysis.

9.3 Implications for practice and policy

Given this was a pilot study making assertions about the implications on practice and policy may seem premature. However there are some important issues highlighted by this study. For those in practice it reiterates the ongoing issue that patients with asthma underplay symptoms and impact on daily life, and a need to actively elicit a true understanding of symptoms during reviews. Worryingly the focus groups and think aloud studies illustrate that practice nurses are increasingly time pressured during reviews to their apparent detriment. Given the findings from the National Review on Asthma Deaths [1] which suggest primary care needs to do more to support self-management, and the importance of the quality of the relationship between patients and providers at influencing levels of adherence and outcomes suggests that this is an area where improvements can be made.

My literature review and qualitative work confirm an ongoing appetite for digital self-management interventions, by both patients and health professionals. I have demonstrated that following the MRC Guidance is feasible and I believe following it has enhanced the intervention developed, such that it shows promise already from the pilot study. The benefits of undertaking a pilot study first are demonstrated by the recruitment being more difficult than we anticipated, and also our finding that spirometry in this way was not feasible. Further exploration of recruitment strategies would be worthwhile before progression to a full scale RCT, as would consideration to proposed strategies for engaging potential end users in the intervention in real life post trial settings.
9.4 Overall Conclusion

There is ever increasing interest in the potential of digital interventions in the healthcare setting, yet how best to utilise this technology in the field of asthma is not yet clear [8]. Suboptimal self-management in asthma continues to contribute to poor outcomes globally, and the need for improving self-management is clear, particularly given evidence of increasing prevalence [5] [1].

I have fully described the development and content of this intervention in an article recently published by BMC Medical Informatics & Decision Making [168]. This transparency allows other researchers, policy makers and practitioners to fully understand and build on this work.

Given that this pilot trial already shows some statistically significant results, it merits further development and evaluations. However some important issues need to be addressed before doing so, in particular recruitment and implementation strategies need further consideration before a definitive evaluation in a full scale RCT. This thesis adds to the body of literature in this ever advancing field of research. I argue within this thesis that researchers developing interventions to support self-management in individuals with mild to moderate asthma should focus on low intensity interventions (ideally with multiple behaviour change techniques) that work independently from health professionals, and further research is needed to confirm whether such interventions do indeed demonstrate more sustained use in real life settings and are cost effective.
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Appendix 1

A Randomized trial of an Asthma Internet Self-management Intervention (RAISIN): study protocol for a randomized controlled trial

Deborah Morrison¹, Sally Wyke², Neil C Thomson³, Alex McConnachie⁴, Karolina Agur¹, Kathryn Saunderson¹, Rekha Chaudhuri³ and Frances S Mair¹*

Abstract

Background: The financial costs associated with asthma care continue to increase while care remains suboptimal. Promoting optimal self-management, including the use of asthma action plans, along with regular health professional review has been shown to be an effective strategy and is recommended in asthma guidelines internationally. Despite evidence of benefit, guided self-management remains underused, however the potential for online resources to promote self-management behaviors is gaining increasing recognition. The aim of this paper is to describe the protocol for a pilot evaluation of a website ‘Living well with asthma’ which has been developed with the aim of promoting self-management behaviors shown to improve outcomes.

Methods/Design: The study is a parallel randomized controlled trial, where adults with asthma are randomly assigned to either access to the website for 12 weeks, or usual asthma care for 12 weeks (followed by access to the website if desired). Individuals are included if they are over 16-years-old, have a diagnosis of asthma with an Asthma Control Questionnaire (ACQ) score of greater than, or equal to 1, and have access to the internet. Primary outcomes for this evaluation include recruitment and retention rates, changes at 12 weeks from baseline for both ACQ and Asthma Quality of Life Questionnaire (AQLQ) scores, and quantitative data describing website usage (number of times logged on, length of time logged on, number of times individual pages looked at, and for how long). Secondary outcomes include clinical outcomes (medication use, health services use, lung function) and patient reported outcomes (including adherence, patient activation measures, and health status).

Discussion: Piloting of complex interventions is considered best practice and will maximise the potential of any future large-scale randomized controlled trial to successfully recruit and be able to report on necessary outcomes. Here we will provide results across a range of outcomes which will provide estimates of efficacy to inform the design of a future full-scale randomized controlled trial of the ‘Living well with asthma’ website.

Trial registration: This trial is registered with Current Controlled Trials ISRCTN78556552 on 18/06/13.

Keywords: Asthma, Self-management, Adherence, E-health, Randomized controlled trial, Complex intervention, Inhaled corticosteroids, Behaviour change
Background

Asthma is common, affecting an estimated 300 million people worldwide [1]. The financial costs associated with asthma care continue to increase [2], while care remains suboptimal - patients continue to overestimate their asthma control, tolerating more symptoms and greater limitations than necessary [3,4]. Promoting self-management, including the use of asthma action plans, along with regular health professional review has been shown to be an effective strategy leading to improved outcomes including improved quality of life, lower rates of healthcare contacts, and fewer days off work and school, and is a recommendation in worldwide asthma guidelines [5-9]. Self-management support aims to improve outcomes in a number of ways: better recognition of deterioration of symptoms, more appropriate responses to exacerbations, and optimizing adherence to medication [10]. Improving adherence to inhaled corticosteroids is crucial to avoid exacerbations, improve day to day control, and reduce the risk of hospitalization and death [11]. Adherence to treatments in many chronic illnesses is low and asthma is no exception [12,13]. Research into non-adherence suggests several rationales, but in common with other chronic conditions recurring themes relate to doubts about the need for the medication in the first place, and concerns about potential side-effects of treatments [12,14].

Despite evidence of benefits, guided self-management remains underused [9-11]. Online interactive tools to support asthma self-management in general have been trialed out with the UK and there is increasing evidence that they may be safe and effective, enabling patients to take a more proactive role, improving asthma quality of life scores and symptoms (and in some cases forced expiratory volume in 1 second (FEV1)) [15-18], and potentially demonstrating cost-effectiveness [19]. This suggests that making effective use of available technologies may have the potential to increase uptake of self-management behaviors in those with asthma, without additional cost. How best to achieve this is still not clear [20].

‘Living well with asthma’ resource development

We developed an online resource ‘Living well with asthma’ which aims to promote optimal self-management behaviors known to lead to improved outcomes. Exploratory focus group discussions with adults with asthma and primary care nurses clarified the key features deemed most important in a website. These data, along with a preceding literature review [20], informed the initial development of a prototype of the website. The actual content of the pages within the website was developed and refined iteratively with input from adults with asthma, practice nurses, general practitioners, a sociologist, human computer interactions researchers, respiratory physicians, and a health psychologist. Further refinement of the content was undertaken using ‘Think aloud’ studies with adults with asthma. These were undertaken by DM, and participants fed back in real time their views on the contents and usability. Initially this was on paper mock-ups of proposed web pages, and latterly on actual ‘Living well with asthma’ webpages. ‘Think aloud’ studies are a recognized method of gaining information about users’ views in real time as they navigate around a website, providing information about usability and feeding into further development and refinement of the website [21,22]. The ‘Living well with asthma’ website was developed as a standalone resource which should complement face-to-face asthma reviews, but does not require health professional involvement.

A full description of the website development will be available in a forthcoming publication.

Rationale for the evaluation methods

Guidance for the development of complex interventions recommends pilot and feasibility studies prior to formal evaluations [23,24]. A pilot study is a version of the main study that is run in miniature to test whether the components of the main study can all work together [25], whereas a feasibility study is used to estimate important parameters that are needed to design the main study, such as ease of recruitment, standard deviations of outcome measures, and follow-up rates [25,26]. This study aims to address both issues. Feasibility and piloting are essential to ensure that planned progression to a full-scale randomized controlled trial (RCT) is appropriate in the first place and if it can be undertaken with appropriate power to achieve definitive results. This early evaluation must be broad enough to provide information both about how a full-scale RCT may work in practice but should also have consideration for how the resource may be used beyond the evaluation. Feasibility is investigated through measuring recruitment and retention rates and collecting usability data about the website itself. Measuring clinical outcomes will allow for the collection of important data on the efficacy of the intervention and for the estimation of effect sizes in any future larger RCT.

Study aims

This study aims firstly to assess the feasibility of conducting a RCT of the clinical effectiveness of an online asthma resource aimed at promoting adherence in adults with poorly controlled asthma, using the ‘Living well with asthma’ resource. Secondly, as a pilot study the aim is to provide estimates of recruitment and retention rates, as well as estimates of the variability of clinical and behavioral outcome measures to inform power calculations for a definitive trial. The study will collect a
range of information about the way the intervention was used, including but not limited to: the most and least visited pages, the length of time the intervention was accessed, and how often it was accessed. Finally, this pilot and feasibility study also aims to identify any potential problems to be addressed, and allow for further development of the resource, before a further evaluation.

We hypothesize that this intervention, which has been designed with end user involvement and aims to improve adherence to therapy using multiple strategies (educational information, attitudinal arguments, self-monitoring, and reminders), will result in improved symptom control and quality of life measures in adults with asthma.

**Methods/Design**

**Ethical approval and trial registration**

Ethical approval for this study was granted by the West of Scotland Research Ethics Committee (ref 13/WOS/004) in March 2013. All participants provided written informed consent. The trial was conducted in accordance with national laws, Good Clinical Practice guidelines and the Declaration of Helsinki 2002. This trial is registered with Current Controlled Trials ISRCTN78556552.

**Recruitment, randomization and blinding**

Participants are primarily being recruited from primary care practices within the Greater Glasgow and Clyde health board area and from posters in public places. We aim to recruit 50 participants in total. See Table 1 for full eligibility criteria.

Consenting participants fulfilling our inclusion and exclusion criteria are being randomized using a third party automated telephone interactive voice response system. Participants will self-complete all questionnaires. Due to the nature of the intervention the blinding of the researcher is not practical, however data will be entered and managed by the Robertson Centre for Biostatistics (RCB), University of Glasgow, and the researcher will take no role in this. The data will be analyzed by a researcher blinded to the allocation of the groups.

**Intervention**

This is a parallel, two arm RCT. See study flow chart (Figure 1) and SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) checklist (Additional file 1) for further details. The duration of participation is 12 weeks from randomization. Those randomized to the intervention arm will have access to a purpose-built website with the aim of facilitating adherence to asthma medications for 12 weeks. This will include the following five areas: a) allow users to gain understanding of their current degree of asthma control and how they can improve it, specifically by optimizing their use of prescribed medication; b) challenge attitudes and concerns around taking medications for asthma; c) learn how to get the most out of their annual asthma review; d) prompt those who do not have one to seek an asthma action plan to be filled in with a health professional; e) prompt those who do not have one to seek an asthma action plan to be filled in with a health professional; e) send reminders to participants such as to get the flu vaccine or to order inhalers (participants can opt out of this aspect).

This resource will not advise medication changes directly, but if indicated, may suggest making an appointment with a nurse or doctor for review. Clear advice will be presented for seeking help in an emergency.

**Control group**

Those randomized to usual care will be advised to continue to manage their asthma as they would usually. After the follow-up visit at 12 weeks, participants in the control group will be offered 12 weeks of access to the website if they choose.

**Outcomes**

**Primary endpoints**

The primary endpoints for this study are: recruitment and retention rates at 12 weeks from baseline, web usability, and changes at 12 weeks from baseline for ACQ [27] and AQLQ [28] scores. Recruitment and retention rates will be measured as well as usage data at 12 weeks, including number of times users logged in and total length of time logged in, number of times individual pages were viewed, and length of time spent on each page.

**Secondary endpoints**

The first secondary endpoint for this study will be changes at 12 weeks from baseline for Patient Activation Measure (PAM) score [29], EQ-5D score (generic measure of health related quality of life) [30], the Morisky Medication Adherence Scale (MMAS) [31], lung function (via pre bronchodilator spirometry FEV1, FEV1/FVC (forced vital capacity), peak expiratory flow (PEF) performed to American Thoracic Society (ATS) standards.

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**Table 1 Inclusion and exclusion criteria**

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<td>1. Written informed consent</td>
<td>1. Unstable asthma</td>
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<td>2. Age 16 years or older</td>
<td>2. Presence of active lung disease other than asthma</td>
</tr>
<tr>
<td>3. Diagnosis of asthma by a health professional and duration of asthma symptoms ≥ 1 year.</td>
<td>3. Mental impairment or language difficulties that make informed consent impossible.</td>
</tr>
<tr>
<td>4. Asthma Control Questionnaire score (6 questions version) greater than or equal to 1 (suggesting poorly controlled asthma)</td>
<td>4. Terminal illness</td>
</tr>
<tr>
<td>5. Ability to access the internet (excluding via smart phone or tablet)</td>
<td>5. Cognitive impairment.</td>
</tr>
</tbody>
</table>
The second secondary endpoint will be changes in the Problematic Experiences of Therapy Scale (PETS) [34] score at 12 weeks in the intervention group only. The third secondary endpoint will be self-reported healthcare utilization including: routine visit to GP or practice nurse because of asthma, visit to GP because of asthma requiring oral steroids, hospital admission (and length of stay) because of asthma requiring oral steroids, emergency or out of hours’ visit because of asthma requiring oral steroids, and emergency or out of hours’ visit of patients to the GP or GP visit to patient at home because of asthma requiring oral steroids. The fourth secondary endpoint will be self-reported medication utilization including: changes in the level of adherence to prescribed preventer medications, changes to the average number of reliever puffs taken per week, intensification of treatment, or step-up of asthma medications (as defined by British Thoracic Society/Scottish Intercollegiate Guidelines Network (BTS/SIGN) guidelines, and step-down of asthma medications (as defined by BTS/SIGN guidelines).

Statistical considerations and data handling
While this study is not powered to detect differences in clinical measures, we will report estimates of effect sizes with a 95% confidence interval. The primary objectives...
include determining recruitment and retention rates to inform the feasibility of running a full-scale trial. We shall recruit 50 participants to estimate these quantities with reasonable precision. For example, if we invite 100 participants to recruit 50, the recruitment rate would be estimated with a confidence interval of ±10%. Patient characteristics and outcomes will be summarized at baseline, at follow-up, and as changes over baseline. Study groups will be compared using baseline-adjusted linear regression (analysis of covariance (ANCOVA)). The effects of baseline and intermediate data on patient outcomes will be explored using linear regression. The variability of outcome data will be used to estimate the sample size required for a definitive study.

Data management
The RCB, part of the Glasgow Clinical Trials Unit (a fully registered UKCRN Clinical Trials Unit) are managing the randomization procedures and the trial data. Case report forms (CRF) will be used to collect study data. The CRF has been developed by the researcher and the RCB. The RCB are responsible for collating study data.

Trial management group and patient safety
The routine management of the trial will be coordinated by the trial management group. This will comprise the chief investigator (DM) and four co-investigators (FM, SW, NT, and AM). This group will monitor the progress of the trial to ensure that the protocol is adhered to. This group will meet bimonthly, with monthly recruitment reports via email. Any changes to the study protocol will be following agreement with the trial management group, and subject to approval from Research and Development at NHS Greater Glasgow and Clyde, and the West of Scotland Research Ethics Committee, where required.

The study will end when the trial management group agrees that either the planned sample size has been achieved or the recruitment is so poor that completion of the trial is not feasible.

Only adverse events that are outcome measures will be recorded. All serious adverse events (SAEs) will be recorded at follow-up. All SAEs will be assessed for causality, expectedness, and severity. This assessment is the responsibility of the chief investigator (CI). The trial team will record all SAEs. The CI will endeavor to obtain sufficient information to determine the causality of the adverse event and must provide an opinion of the causal relationship between each SAE and the study intervention. The accumulated SAEs will be sent to the sponsor and the West of Scotland Research Ethics Committee in an annual safety report. Detailed records of all SAEs will be held in the trial master file.

Annual safety reports
It shall be the responsibility of the trial management group on behalf of the sponsor to submit, once a year throughout the clinical trial, or on request, a safety report to the West of Scotland Research Ethics Committee.

Discussion
The increasing burden of chronic disease on healthcare providers is well known, and promoting self-care is a strategy for shifting this burden away from healthcare providers. The Internet may provide a cost-effective medium for doing this. Piloting of complex interventions is considered best practice and will maximize the potential of any future full-scale RCT to successfully recruit and be able to report on necessary outcomes. Here we report on feasibility outcomes such as recruitment, retention, and usability of the intervention being investigated, and undertake piloting of an intervention which will aim to determine clinical efficacy.

Trial status
Recruitment was initiated in June 2013, with the first patient randomized in September 2013, and is ongoing as of February 2014.

Additional file

Additional file 1: SPIRIT Checklist as appropriate to a non-CTIMP (Controlled Trial of Investigational Medicinal Product).

Abbreviations
ACQ: Asthma Control Questionnaire; AQLQ: Asthma Quality of Life Questionnaire; ATS: American Thoracic Society; BTS/SIGN: British Thoracic Society/Scottish Intercollegiate Network; CI: Chief Investigator; CRF: Case Report Form; CTIMP: Controlled Trial of Investigational Medicinal Product; FeNO: Fractional Exhaled Nitric Oxide; FEV1: Forced Expiratory Volume in 1 second; FVC: Forced Vital Capacity; GP: General Practitioner; MMAS: Morisky Medication Adherence Scale; PAM: Patient Activation Measure; PEF: Peak Expiratory Flow; PETs: Problems of Experienced Therapy Scale; RCB: Robertson Centre for Biostatistics; RCT: Randomized Controlled Trial; SAE: Serious Adverse Event.

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
DM developed and designed the trial in collaboration with FM, SW, NT, AM, RC. Recruitment of practices or patients was undertaken by DM, KA, KS and FM. Data collection was undertaken by DM, KA and KS. DM wrote the first draft of the protocol and refined it based on comments and feedback from all other authors. All authors read and approved the final manuscript.

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Appendix 2

Details of development of the resource for adults with asthma in the RAISIN (randomized trial of an asthma internet self-management intervention) study

Deborah Morrison¹, Frances S. Mair¹*, Rekha Chaudhuri², Marilyn McGee-Lennon³, Mike Thomas⁴, Neil C. Thomson², Lucy Yardley⁵ and Sally Wyke⁶

Abstract

Background: Around 300 million people worldwide have asthma and prevalence is increasing. Self-management can be effective in improving a range of outcomes and is cost effective, but is underutilised as a treatment strategy. Supporting optimum self-management using digital technology shows promise, but how best to do this is not clear. We aimed to develop an evidence based, theory informed, online resource to support self-management in adults with asthma, called ‘Living well with Asthma’, as part of the RAISIN (Randomized Trial of an Asthma Internet Self-Management Intervention) study.

Methods: We developed Living well with Asthma in two phases. Phase 1: A low fidelity prototype (paper-based) version of the website was developed iteratively through input from a multidisciplinary expert panel, empirical evidence from the literature, and potential end users via focus groups (adults with asthma and practice nurses). Implementation and behaviour change theories informed this process. Phase 2: The paper-based designs were converted to a website through an iterative user centred process. Adults with asthma (n = 10) took part in think aloud studies, discussing the paper based version, then the web-based version. Participants considered contents, layout, and navigation. Development was agile using feedback from the think aloud sessions immediately to inform design and subsequent think aloud sessions. Think aloud transcripts were also thematically analysed, further informing resource development.

Results: The website asked users to aim to be symptom free. Key behaviours targeted to achieve this include: optimising medication use (including inhaler technique); attending primary care asthma reviews; using asthma action plans; increasing physical activity levels; and stopping smoking. The website had 11 sections, plus email reminders, which promoted these behaviours. Feedback on the contents of the resource was mainly positive with most changes focussing on clarification of language, order of pages and usability issues mainly relating to navigation difficulties.

Conclusions: Our multifaceted approach to online intervention development underpinned by theory, using evidence from the literature, co-designed with end users and a multidisciplinary panel has resulted in a resource which end users find relevant to their needs and easy to use. Living well with Asthma is undergoing evaluation within a randomized controlled trial.

Keywords: Asthma, Self-management, Adherence, E-health, Randomized controlled trial, Complex intervention, Inhaled corticosteroids, Internet, Behaviour change, Lifeguide

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Background

Asthma is common, affecting 300 million people worldwide, and its prevalence is increasing; an estimated additional 100 million people will have asthma by 2025 [16]. Despite increasing costs associated with asthma [2], care remains suboptimal, with many patients tolerating symptoms and lifestyle limitations unnecessarily, due to suboptimal use of proven available therapies [11, 26, 29, 32].

Supporting optimum self-management by providing relevant self-management education including how to use an asthma action plan (AAP), regular health professional review, and optimal use of medications has been shown to have positive effects on a range of asthma outcomes such as improved quality of life, lower rates of healthcare contacts, and fewer days off work and school [7]. Promoting self-management is a recommendation in worldwide asthma guidelines [4, 8]. Despite this, self-management as a treatment strategy remains underused [8, 32, 34].

Recently, new information and communication technologies (ICTs) have been proposed as a means to improve asthma self-management uptake. We conducted a meta-review [22] which showed that online interactive resources to support self-management of asthma can be safe and effective at improving some outcomes such as markers of self-care, activity limitation, quality of life and medication use. However, interventions were poorly described and it was impossible to extract generalisable lessons about the key ‘active ingredients’ of interventions. This challenge has previously been recognised by Michie et al. [20] who in response have developed a taxonomy of behaviour change techniques (BCTs) which they propose researchers can use to describe interventions, in order to overcome the lack of a systematic way of determining the ‘active ingredients’ of a complex interventions [21].

Traditionally, development of online interventions has been resource intensive with each intervention requiring to be programmed individually by a team of programmers from scratch—a barrier to internet based interventions being cost-effective when compared to face-to-face or paper alternatives. A team in Southampton who have recognised the increasing potential for delivering health care online have developed an open access software package called LifeGuide [10, 38, 41]. LifeGuide aims to allow researchers from a non-computer programming background to more easily and flexibly create and modify internet-delivered interventions. It has been used successfully in a number of health related interventions [3, 33, 38]. A key design feature of LifeGuide is that it allows researchers to easily test parts of an intervention and immediately modify and improve it based on the findings, and to trial it in the development phase.

Here we describe the development and optimisation of the Living well with Asthma website which we developed using the LifeGuide open access software package guided by the updated MRC guidance for the development and evaluation of complex interventions [18]. The Living well with Asthma website is currently undergoing evaluation in a randomised controlled trial (RCT) called RAISIN (Randomized Trial of an Asthma Internet Self-Management Intervention) (ISRCTN 78556552) [23].

Methods

To develop the Living Well with Asthma website we followed the steps outlined in the updated MRC guidance which recommends that intervention development should be systematic, include review of the evidence, be theory based, and incorporate feasibility or user testing [18]. In this section we describe the two phases of work we undertook to incorporate these steps. Ethical approval was granted from the West of Scotland Research Ethics Committee (12/WS/0068), and all participants provided informed consent.

Phase 1: intervention planning

Phase 1 describes the process of developing a ‘first draft’ of the website. This phase consisted of three main work packages (WP), all overseen by a multidisciplinary ‘expert panel’ made up of 3 general practitioners, a respiratory physician, a health psychologist, a social scientist, and a human-computer-interaction researcher.

Work package 1—understanding the evidence & incorporating theory (scoping review and expert panel)

Campbell et al. [5] describe 5 key tasks involved in defining and understanding the ‘problem’ that your intervention is aiming to solve, namely: 1) defining and quantifying the problem; 2) identifying who is mostly likely to benefit; 3) understanding the pathways which contribute to the problem; 4) consideration of whether (and how) these pathways are amenable to change; 5) and attempting to quantify the potential for improvement. We did a brief scoping review of the literature and used the experience of our expert panel to work through these tasks. We identified a list of features that a resource should have, incorporating recommended behaviour change concepts [25].

Work package 2—getting user perspectives on a web resource (focus groups)

In order to investigate the plausibility of this list with potential end users we convened 2 focus groups, consisting in total of 9 adults with asthma (6 female, 3 male), and 4 practice nurses who undertake asthma reviews. Recruitment was undertaken using a range of sources: primary care, Asthma UK Research and Policy volunteers, Chest Heart Stroke Scotland volunteers and a secondary care asthma clinic. Adults aged 18 and over were eligible provided they had a diagnosis of asthma...
and could provide informed consent. There was no upper age limit on participation. Participants could agree to participate in a focus group, up to two think aloud studies (described in phase 2), or both. Focus groups were held at the Department of General Practice & Primary Care, University of Glasgow, and were audio recorded and transcribed. We used the implementation theory Normalization Process Theory (NPT) [24] to inform the topic guide for these focus groups (Fig. 1). This theory was used as it is being increasingly advocated as a means to understand implementation processes and enhance the implementability of interventions [17, 24]. Discussion focused on the perceived barriers and facilitators to sustained use of an online resource to support self-management. This consideration of implementation issues at such an early stage is a key message from the MRC guidance. Our list of potential features derived from WP 1 was explored using questions generated from our topic guide (Fig. 1) and we sought suggestions for additional features. The focus groups were transcribed and any statements which were barriers or facilitators to self-management were extracted, along with any suggestions for features to include in our website.

Work package 3—developing a draft version of the website (expert panel)

Using information gathered from WP 1 and 2, the list of suggested features to include in the website was reviewed and refined iteratively. As low fidelity prototype pages were generated (initially using Microsoft Word or PowerPoint) (also referred to as draft pages) they were reviewed initially by those in the panel with a clinical background to ensure the content was factually correct. Subsequently the pages were shown to members of the expert panel with specific expertise in behaviour change theory to ensure maximum opportunity for promoting behaviour change was incorporated into each page or section, using the behaviour change concepts agreed on from WP1 [25]. From this a draft version of each potential webpage was finalised, ready for think aloud study evaluation.

Phase 2: iterative refinement of the resource contents of the website (think aloud studies and expert panel)

Draft pages developed at the end of Phase 1 were gradually translated into interactive webpages with input from potential end users in the form of think aloud studies, and review by the expert panel. While LifeGuide can be used by researchers with no computing science background, due to time constraints, a programmer transferred the majority of the draft pages into LifeGuide initially. Think aloud studies were undertaken by the first author at either the participant’s home, or the Department of General Practice & Primary Care, University of Glasgow, depending on individual participant preference. Participants were recruited from the same pool as the focus groups, and they could participate in a maximum of two think aloud studies. There were two waves of think aloud studies: the first 4 used draft webpages still on paper or PowerPoint slide, the latter 6 were undertaken completely using the prototype webpages on LifeGuide. Participants were asked to say whatever they thought or felt about what they were seeing, with prompts and questions used to elaborate on responses. The participants were then encouraged to voice any additional suggestions or opinions to improve the resource, for example what they liked and disliked, what was intuitive and what was not, and how they envisaged using such a website in real life in the future. The majority of the findings from the think aloud studies were acted upon immediately after the session by the researcher doing the think aloud studies, in order to progress the resource ready for the subsequent think aloud study. We also thematically analysed the transcriptions of the think aloud studies with the aim of providing information for further development of the resource following the pilot RCT.

Thematic analysis was undertaken using a coding frame developed by DM. Both DM and SW independently coded the first 2 transcripts, and results compared, after which DM coded the remaining transcripts. Comments were noted to be either a positive comment, where the user liked or identified with what they saw, or a negative comment where the user disliked or disagreed with what they saw, or where the user suggested an improvement or alternative way of presenting the data. The final version of the Living well with Asthma website was formally mapped to Michie and colleagues latest BCT taxonomy [21] in order to describe which BCTs were present. Every page of the website was reviewed by the first author (DM), and where relevant a BCT was assigned. These were subsequently reviewed by SW. We did this to provide a reliable record of the content of this behaviour change intervention, and to confirm that we included a range of BCTs as planned.
**Results**

This results section describes the key steps in our website development.

**Phase 1: initial planning stages**

**Work package 1—understanding the evidence & incorporating theory (scoping review and expert panel)**

The planning stage focussed on the 5 key tasks outlined by Campbell et al. [5]. This process helped us understand that the main problems we aimed to address centred round: 1) the suboptimal use of preventative therapies; 2) the high levels of symptom burden; and 3) the low rates of attendance at asthma reviews and use of asthma action plans. We anticipated that concepts derived from behaviour change theory should help us address these identified problems, and the full results of WP 1 are described in Table 1.

**Work package 2—getting user perspectives on a web resource (focus groups)**

We shared our results from Table 1 with potential end users in the focus groups. Excluding the practice nurses the average age of participants was 41 years (range 23 to 56). Six participants were female, 4 male, and included participants from highest and lowest deprivation deciles (median 4, IQR 1, 8). Table 2 describes the participants, illustrating which focus group (or think aloud study) they participated in. Participants were recruited from Asthma UK volunteers (n = 5), primary care (n = 3) and hospital asthma clinic (n = 2). Barriers to optimum self-management identified by focus groups included not accepting diagnosis, difficulties keeping track of medications and remembering to order more, and the length of time between asthma reviews resulting in knowledge loss. Facilitators to using an online resource included staggering of information, a resource to bridge the gap between annual reviews and reinforcement of material covered, provision of email reminders i.e. ordering medication and flu vaccinations, resource being promoted during annual reviews and making users aware of different types of inhalers available and importance of finding one that suits.

These barriers and facilitators were combined with those from the literature (including asthma guidelines) to provide a list of suggested features to include in a resource. This process is shown in full Additional file 1, illustrating the rationale for the contents of the website.

**Work package 3—developing a draft version of the website (expert panel)**

By the end of WP 1 and 2 we established there were 6 main behaviours we wanted to promote within the website:

- Attend for regular asthma review
- Use asthma action plans
- Increase physical activity
- Stop smoking

The expert panel reviewed the list of suggested features from Additional file 1 which led to the removal of four: a diary for tracking medication use, a diary for tracking peak expiratory flow (PEF) rate, a tailored action plan and a dedicated family & friends sections. The expert panel felt that evidence and personal experience suggested that use of diary tools was rarely sustained except by a few very motivated individuals. Instead regular prompts to think about current asthma symptoms based on the ‘Royal College Physicians 3 Questions’ (RCP 3Q) screening tool [27] was incorporated throughout the resource and in the automated emails. This asks the user about difficulty sleeping because of asthma, asthma symptoms during the day, and interference with usual activities. If users answer yes to even one question then further assessment of asthma control is indicated [28, 35]. Action plans work best when personalised to the individual [6] and the IT requirements of a truly tailored action plan was considered beyond the scope of this project. Instead a section was dedicated to promoting the use of action plans, and encouraging individuals to visit their health professional to agree one if they didn’t have one. Rather than a dedicated family and friends section the importance of positively involving family and friends was discussed in general terms.

By the end of Phase 1 we had developed paper based versions of the web pages ready for consideration by the expert panel and for use in think aloud studies.

**Phase 2: iterative refinement of the resource contents of the website (think aloud studies and expert panel)**

Eleven think aloud studies (see Table 2 for participant details) were conducted although one study (TA 08) was not completed as the website was not compatible with her type of computer which converted website text into braille (BrailleNote). Four of the 11 studies were undertaken in the participants’ own home. Three of the participants (participants 3, 4 and 10) undertook 2 studies each. Each think aloud interview covered a slightly different range of topics as the resource was developed iteratively (Table 3). Table 4 explains the nature of the changes made during this phase as a result of input from the think aloud participants and the expert panel.

Thematic analysis of the think aloud transcripts identified three main thematic categories: 1) ‘content’—the actual words on the pages, and how relevant and understandable the information was; 2) ‘layout and navigation’—the layout of pages or sections, and how easy it was to navigate around sections; and 3) ‘user experience’.
### Table 1 Defining and understanding the problem

<table>
<thead>
<tr>
<th>Key Tasks [5]</th>
<th>Commentary relating tasks to LWWA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Task 1: Define and quantify the problem</strong></td>
<td>Optimum self-management of asthma is an underused, yet proven treatment strategy that improves a range of asthma outcomes (fewer visits to emergency room, hospitalisations, unscheduled visits to doctors, and days off work and school, reduces nocturnal asthma and improves quality of life) [7]. People with asthma have:</td>
</tr>
<tr>
<td></td>
<td>1) Suboptimal use of preventative therapies. Adherence to therapies in long term conditions is around 50 % [39]. Low use of preventative (inhaled corticosteroids (ICS)) therapies and high use of short acting beta agonists (SABA) reliever inhalers, is a pattern commonly seen which is associated with poorer asthma control [29].</td>
</tr>
<tr>
<td></td>
<td>2) High levels of symptom burden (46 % daytime symptoms and 30 % nocturnal symptoms) [30], with lack of recognition of scope for improvement: 50 % of patients reporting severe persistent symptoms report their own asthma as being completely or well controlled [30]. This results in people with uncontrolled or deteriorating asthma not seeking timely medical advice.</td>
</tr>
<tr>
<td></td>
<td>3) Suboptimal attendance at asthma reviews with low use of asthma action plans (AAPs) [13, 32] as evidenced by the National Review of Asthma Deaths (NRAD) where only 23 % of those who died having been provided with an AAP [32], and attendance at asthma reviews in Scotland was only 65 %.</td>
</tr>
<tr>
<td><strong>Task 2: Identify and quantify the population most affected, most at risk, or most likely to benefit from the intervention</strong></td>
<td>The Global Initiative for Asthma (GINA) guidelines lists risk factors for poor asthma outcomes [8]:</td>
</tr>
<tr>
<td></td>
<td>• Uncontrolled asthma symptoms</td>
</tr>
<tr>
<td></td>
<td>• Increased use of short acting beta agonist (SABA) e.g. reliever therapy</td>
</tr>
<tr>
<td></td>
<td>• Inadequate inhaled corticosteroids (ICS), including poor technique.</td>
</tr>
<tr>
<td></td>
<td>• Low FEV&lt;sub&gt;1&lt;/sub&gt; (especially if &lt;60 % predicted)</td>
</tr>
<tr>
<td></td>
<td>• Major psychological or socioeconomic problems</td>
</tr>
<tr>
<td></td>
<td>• Smoking</td>
</tr>
<tr>
<td></td>
<td>• Comorbidities: obesity, rhino-sinusitis, food allergy</td>
</tr>
<tr>
<td></td>
<td>• Previous exacerbations or intensive care admissions for asthma</td>
</tr>
<tr>
<td></td>
<td>The majority of these factors are related to uncontrolled asthma symptoms, and therefore a key way of identifying those most likely to benefit is to target those with uncontrolled asthma symptoms.</td>
</tr>
<tr>
<td><strong>Task 3: Understand the pathways by which the problem is caused</strong></td>
<td>With reference to problems outlined in task 1:</td>
</tr>
<tr>
<td></td>
<td>1) Reasons for low adherence to asthma therapies are often related to concerns about side effects, or perceptions that they don’t need to be on treatments [12].</td>
</tr>
<tr>
<td></td>
<td>2) The global asthma insights and reality surveys [29] provides evidence of suboptimal asthma control and suggests reasons for it. First, people with asthma overestimate how controlled their asthma is, therefore don’t consider themselves to be candidates for gaining improvement with asthma treatments. Second, those who do acknowledge they have symptoms and limitation of activities accept them as unavoidable consequences of having asthma.</td>
</tr>
<tr>
<td></td>
<td>3) Patients reasons for not attending asthma reviews revolve around feelings that their asthma is not serious enough [9]. Asthma Action plans are underused for several reasons [31]:</td>
</tr>
<tr>
<td></td>
<td>i) Differences in beliefs and attitudes between health care professionals and people with asthma.</td>
</tr>
<tr>
<td></td>
<td>ii) Perceived irrelevance of AAPs of the part of those who would potentially benefit from them</td>
</tr>
<tr>
<td></td>
<td>iii) Health professionals only offer AAPs to select groups of patients (e.g. with well controlled asthma, or those with higher levels of educational achievement).</td>
</tr>
<tr>
<td></td>
<td>In summary, people with asthma often underestimate their symptoms and overestimate their control, not making use of available therapeutic options (medications, AAPs and advice from health professionals). Those who do recognise they have symptoms may not adhere to prescribed medications due to misunderstandings around medication side effects, or perceived benefits of using AAPs.</td>
</tr>
</tbody>
</table>
NVivo software allowed us to generate quantitative data from the think aloud transcripts. Fifty one percent of the comments were positive, 15% negative and 34% containing suggestions for improvement. This suggests that participants felt comfortable criticizing or making suggestions for improvement of the website. Most comments related to the content of pages (78%), and the majority of these were positive (56%). In contrast, most comments about the website layout and navigation were negative (69%) (Fig. 2). This confirmed that the groundwork done in Phase 1 around content had been successful, but that greater emphasis was needed on usability and presentation issues.

**Content—making the website relevant and understandable**

Participants were positive about the contents, and in particular the 'level' it was aimed at:

"it's very clear in its intention, a website to help you stay healthy and manage your asthma better that's

### Table 1 Defining and understanding the problem (Continued)

| Task 4: Explore whether these pathways may be amenable to change and, if so, at which points | With specific reference to the three ‘problems’ outlined in Task 1:
|                                                                                       | 1) Prompting users to consider reasons why they don’t take medications regularly (barriers) and consider strategies to overcome these barriers. Providing information about benefits of inhaled corticosteroids, challenging misconceptions and negative beliefs. Focussing on benefits meaningful to individuals such as fewer days off work, managing that exercise class etc. Providing instructions (ideally including videos) to demonstrate correct inhaler technique.
|                                                                                       | 2) Promoting the message that users should be aiming for no symptoms. Providing information to challenge the belief that having asthma symptoms is normal, and asking validated questions to determine if users are currently putting up with symptoms, providing feedback on response. Prompting users to recognise if they avoid activities due to their asthma, or are limited in everyday tasks such as housework, gardening, visiting friends. Turn these limitations into ‘goals’ to aim towards, and describing how these goals are achievable for them.
|                                                                                       | 3) Provide information that people who use AAPs and attend for reviews have fewer symptoms and fewer asthma attacks. Provide quotes from practice nurses encouraging attendance for reviews. Remove physical barrier to using AAPs by providing a template that can be taken to health professionals (identical to those provided by local health board).

The expert panel will ensure that behaviour change theory is incorporated into the web page contents and full analysis of behaviour change techniques will be done on final website (Table 6).

### Table 2 Demographics of participants in focus groups and think aloud studies

<table>
<thead>
<tr>
<th>Participant number</th>
<th>FG 1</th>
<th>FG 2</th>
<th>TA 1</th>
<th>TA 2</th>
<th>Female</th>
<th>Male</th>
<th>Age (yrs)</th>
<th>SIMD</th>
<th>Ethnicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>●</td>
<td>●</td>
<td>● (2)</td>
<td>●</td>
<td></td>
<td>44</td>
<td>1</td>
<td>1</td>
<td>White British</td>
</tr>
<tr>
<td>2</td>
<td>●</td>
<td>●</td>
<td>● (3)</td>
<td>●</td>
<td></td>
<td>23</td>
<td>1</td>
<td>1</td>
<td>White British</td>
</tr>
<tr>
<td>3</td>
<td>●</td>
<td>●</td>
<td>● (4)</td>
<td>● (11)</td>
<td></td>
<td>51</td>
<td>8</td>
<td>1</td>
<td>White British</td>
</tr>
<tr>
<td>4</td>
<td>●</td>
<td>●</td>
<td>● (5)</td>
<td>● (9)</td>
<td></td>
<td>46</td>
<td>4</td>
<td>1</td>
<td>White British</td>
</tr>
<tr>
<td>5</td>
<td>●</td>
<td>●</td>
<td>● (6)</td>
<td>●</td>
<td></td>
<td>23</td>
<td>1</td>
<td>1</td>
<td>White British</td>
</tr>
<tr>
<td>6</td>
<td>●</td>
<td>●</td>
<td>● (7)</td>
<td>●</td>
<td></td>
<td>56</td>
<td>8</td>
<td>1</td>
<td>White British</td>
</tr>
<tr>
<td>7</td>
<td>●</td>
<td>●</td>
<td>● (8)</td>
<td>●</td>
<td></td>
<td>55</td>
<td>3</td>
<td>1</td>
<td>White British</td>
</tr>
<tr>
<td>8</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>41</td>
<td>6</td>
<td></td>
<td></td>
<td>White British</td>
</tr>
<tr>
<td>9</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>29</td>
<td>10</td>
<td></td>
<td></td>
<td>White British</td>
</tr>
<tr>
<td>10</td>
<td>●</td>
<td>●</td>
<td>● (1)</td>
<td>● (10)</td>
<td></td>
<td>48</td>
<td>10</td>
<td>1</td>
<td>White British</td>
</tr>
</tbody>
</table>

*refers to adults with asthma participating. Two practice nurses also present in each focus group, details not provided. Number in brackets refers to think aloud study number, participant number 3, 4 and 10 participated in two think aloud studies each. SIMD: Scottish Index of Multiple Deprivation. Range from 1 (most deprived) to 10 (most affluent)
exactly what level I'm at, I don't have a detailed knowledge of what I've got or quite what I've got or quite how to look after it so it's perfect for me.

(Participant 10, TA01)

Users liked and identified with the key messages, for example that people with asthma should be ‘aiming for no symptoms’:

“I like a message of you know that's what you should be aiming for, it might not be what you get right enough but at least you should be aiming for, or aiming for it the majority of the time, you know but you can if, you know going to have relapses, but I think that that's really good because I don't think many people actually say that to you to be honest.”

(Participant 1, TA02)

“That's good to know because again I just was putting up with it like if I was, if I wasn't being able to breathe I would just be like oh I'm just having a bad day rather than being like 'oh I should really be on the brown inhaler to stop this from happening';

(Participant 3, TA04)

While there was universal agreement that quotes from patients and practice nurses were desirable within the website there was some disagreement about how they should be presented:

“But I would give them maybe slightly more weight if they weren't anonymous bizarrely. And it's a real living patient that is living with asthma. And that kind of makes it more of a human.” (Participant 10, TA01)

In the following think aloud study this point was brought up by the interviewer:

“the quotes do you think, would you prefer to see something like female age 53 or is it not relevant?” (researcher)

“It's not relevant to be honest because if I was twenty one and I was reading and they were fifty I would be thinking oh that doesn't apply to me yet. The guy will be reading it and thinking oh that's a woman thing.”

(Participant 1, TA02)

Consequently, we kept quotes in the website but removed descriptions of who said them, as illustrated in Fig. 3.

While patients on the whole agreed with the information provided, the one area where there was scepticism was in regard to how approachable participants’ practices nurses were:

“just trying to imagine sort of sitting down with my asthma nurse and saying I have a goal and this is what I want to achieve, I know what she'd say, she'd say I haven’t got time to discuss this! Let's just stick to the tick boxes shall we?” (Participant 4, TA05)

**Table 3 Think aloud studies—topics covered**

<table>
<thead>
<tr>
<th>Introduction</th>
<th>My asthma</th>
<th>Treatments</th>
<th>Asthma review</th>
<th>Exercise</th>
<th>Concerns</th>
<th>Queries</th>
<th>Stress</th>
<th>Anxiety</th>
<th>Action plan</th>
<th>4 week challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td>TA01</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td></td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>TA02</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>TA03</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td></td>
<td>●</td>
<td>●</td>
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<td>●</td>
</tr>
<tr>
<td>TA04</td>
<td>●</td>
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<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
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<td>●</td>
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</tr>
<tr>
<td>TA05</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
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<td>TA06</td>
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<td>TA07</td>
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<td>TA08</td>
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<td>●</td>
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<tr>
<td>TA09</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
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<tr>
<td>TA10</td>
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<td>●</td>
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<td>●</td>
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<td>●</td>
</tr>
<tr>
<td>TA11</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
</tbody>
</table>

*My asthma section eventually split into 3 sections numbered s1, s2, s3. With s1 being based mainly on the contents reviewed at the first 3 think alouds before recognising need for 3 versions of this section: S1—I have never been prescribed or used a preventer inhaler; S2—I have a preventer inhaler but don’t really use it as prescribed; S3—I have a preventer inhaler and mostly use it as prescribed. TA01 and TA10 were same participant; TA04 and TA11 were same participant; TA05 and TA09 were same participant. TA08 used a BrailleNote computer, which was not compatible with our software so we were unable to complete the Think Aloud study.

Layout and navigation—making the website easy to use

The majority of the comments regarding layout were page specific such as feeling that a given paragraph was too long, and where appropriate were acted on immediately after the think aloud study in preparation for the next one. However the importance of getting the home page right was clearly important to participants and generated discussion.
### Table 4 Changes made during phase 2

<table>
<thead>
<tr>
<th>Section (pages)</th>
<th>Topics</th>
<th>Description of changes made</th>
</tr>
</thead>
</table>
| 1 (13 pages)    | Introduction pages<sup>b</sup>  
Home page | Original one page introduction became 13+ page section.  
- Both TA participants and expert panel highlighted that people with asthma are well known for underestimating their asthma severity, and suggested it was important to challenge this idea right at the start and illustrate to users how this resource could benefit them.  
- First page presented user with questions designed to tease out limitations due to asthma. Then feedback provided for each question user ticked, along with tailored advice about which sections of the resource might benefit them most.  
- Subsequent pages focused on identifying lifestyle goals relevant to users.  
- Other changes included addition of a 'landing' page, combining links to sections to reduce the 'buttons' in the navigation bar from 11 down to 7, and rearranging the home page. |
| 2 (24 pages)    | My Asthma<sup>b</sup> | Initially just one section, but became apparent that resource needed to be more tailored, and preventer therapy use was a good method of stratifying users, so users had to choose one of three options:  
1) I have never used/been prescribed a preventer  
2) I have been prescribed a preventer but don't really use it  
3) I mostly/always take my preventer inhaler as prescribed  
The think aloud study confirmed the contents of this section, with most changes focusing on improving readability, removing repetition and trying to achieve the right balance when explaining negative side effects versus potential benefits of inhaled steroids. |
| 3 (14 pages)    | Treatments | Organization of this section completely altered. It initially took the form of 6 pages users worked through with sideway steps for more information about different treatments.  
Section changed to have:  
- its own homepage (i.e. spoke and wheel layout) which allowed users to go directly to a treatment type without having to work through potentially irrelevant pages.  
- a visual representation of the asthma treatment ladder adapted from the BTS/Sign guidelines.  
We were unable to meet requests to have pictures of individual inhalers. |
| 4 (21 pages)    | Asthma Reviews | Focused on modifying the language used and simplifying messages.  
- Altering layout of both individual pages and order of pages.  
- Main message was to “aim for no symptoms” and this was very well received by users.  
- Included a quiz covering what put people at risk of attacks—this was streamlined and made optional. |
| 5 (5 pages)     | Action Plans | Altered layout and clarity of wording, and quotes added to dilute the very factual nature of the information provided.  
- Added a template to a blank action plan that users could print out and take to their health professional. |
| 6 (17 pages)    | Physical Activity | Initially one generic section with the aim of promoting physical activity but was altered to become tailored to the individual's activity status. |
Table 4 Changes made during phase 2 (Continued)

<table>
<thead>
<tr>
<th>Section</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Common concerns and queries</td>
</tr>
<tr>
<td>18 pages</td>
<td>Originally had 8 concerns and queries, and a further 7 were added addressing topics originally not included as were felt to be covered elsewhere, or had seemed ‘too basic’.</td>
</tr>
<tr>
<td></td>
<td>Reviewing this section served as a reminder that people quickly forget (or have never been told) even basic information about their asthma, and that having it here for those who need it was essential.</td>
</tr>
<tr>
<td></td>
<td>Another major change was the wording of questions. One user commented that questions were just statements and didn’t make it clear than scenarios were amenable to change. So for example ‘I don’t exercise because of my asthma’ was changed to ‘I don’t exercise because of my asthma. Could I?’</td>
</tr>
<tr>
<td>8</td>
<td>Stress &amp; Anxiety</td>
</tr>
<tr>
<td>5 pages</td>
<td>Received mainly positive feedback.</td>
</tr>
<tr>
<td></td>
<td>Links to online resources aimed at reducing stress and anxiety (e.g. online CBT) added.</td>
</tr>
<tr>
<td>9</td>
<td>Take the 4 week Challenge</td>
</tr>
<tr>
<td>8 pages</td>
<td>This section was specifically for users who had chosen option 1 or 2 during the ‘My Asthma’ section.</td>
</tr>
<tr>
<td></td>
<td>Initially much confusion about the nature of the challenge with some users misunderstanding it completely. Thus pages were modified and more explanation added.</td>
</tr>
<tr>
<td></td>
<td>Layout of pages were altered, in particular, to make it clear that there were 4 steps to work through, and it was made clearer how you were progressing through them (e.g. colour strip across the top, which illustrated progress).</td>
</tr>
<tr>
<td></td>
<td>One of the steps to the four week challenge was to anticipate barriers to taking preventer medication regularly and consider some solutions. Template barriers and solutions were provided, and these were added to by the think aloud participants.</td>
</tr>
<tr>
<td>10</td>
<td>Like to stop smoking?</td>
</tr>
<tr>
<td></td>
<td>This section was a link to an external site called ‘StopAdvisor’[19] and therefore not covered during the think aloud studies.</td>
</tr>
<tr>
<td>11</td>
<td>Useful info and links</td>
</tr>
<tr>
<td>1 page</td>
<td>Expanded during the think aloud to include more links to online mental health resources and information about the GP exercise referral scheme.</td>
</tr>
</tbody>
</table>

*Refers to unique pages per section. Some pages are referred to in more than one section, but are only counted once here in the first section they appear

*All users are directed through these two sections at first login, and can optionally visit again during future sessions.

Fig. 2 Type of comment made during think aloud studies
“it doesn’t quite feel like a home page, that’s maybe not helpful. I’m trying to think what the best way to, it looks the same as every other page, I don’t know if you did something different to the header or something like that.” (Participant 4, TA05)

Therefore the home page was modified as illustrated in Fig. 4 in response to comments across the studies.

The second recurring theme related to users ‘knowing where I am’.

“I say I might have said before maybe a little site map you are on step 3 of 9, 4 of 9 and people know where they are going.” (Participant 4, TA09)

As a result it became more obvious which section a user was in at a given time, and within the 4 week challenge section it was made much more obvious how users progressed through the 4 stages of preparing to sign up to the ‘4 week challenge’.

User experiences
After completing the think aloud study users were asked how they might use the website in a real life setting and what would be barriers to its sustained use. Users felt that they would have more confidence in such a resource if a health professional recommended it:

“I guess like in my annual review, if my nurse was like oh have a look at this. Like a wee leaflet or a wee business card or something like that and just was like have a look at that.” (Participant 2, TA03)

This finding is relevant for both future large scale RCTs, and the subsequent implementation and embedding of such a resource.

Completion of this phase resulted in the final website ready for evaluation in the RAISIN trial [23]. Table 5 describes the final contents of the resource, and further sample screenshots are provided in Additional file 2.

BCTs present in website
We incorporated 20 BCTs in our Living well with Asthma website as described in Table 6. The most commonly used BCTs were ‘information about health consequences’ and ‘demonstration of the behaviour’, followed by ‘problem solving’ and ‘instruction on how to perform a behaviour’. We also used ‘goals and planning’ as a key behavioural technique within the website.
Early version of home page:

![Early version of home page](image)

Thank you. Before moving on to talking about your asthma specifically here is some general information about how to use the website.

This is the "home page".

You can get back to the home page at any time by clicking the logo across the top of the page.

When you first log in to the website, after you have filled in some questions you will be taken directly to the "My Asthma" section from this page by pressing the next button.

Once you have viewed the "My Asthma" section you can look at any section you wish. Any time you login again you will be taken straight to this page, and you can visit any section, in any order.

Final version of home page:

![Final version of home page](image)

From this page you can navigate to any section.

Click on any topic area that you are interested in. To return to this page at any time click on the 'Living well with asthma' logo across the top of the page.

Fig. 4 Changes made to home page during Phase 2
We have demonstrated the feasibility of developing an evidence-based, theory guided, user friendly behaviour change intervention in the form of Living well with Asthma—a website to support self-management in adults with asthma. We have been guided by the MRC Framework on developing and evaluating complex interventions, and as a result directed much effort to the key, yet often overlooked, planning stages [5, 18]. We undertook recommended key tasks to guide our development methods [5], see Table 1, through: synthesis of empirical evidence, using expert knowledge and experience, and incorporating theoretical concepts with end user input, to produce an evidence based behaviour change website. Our evidence synthesis highlighted that self-management of asthma is an underused, yet proven, treatment strategy [7] and that people with asthma frequently do not use therapies optimally, tolerate high levels of symptom burden, and do not attend asthma reviews or make use of asthma action plans. This underestimation of symptoms and overestimation of control is a barrier to making use of available therapies. Those who do recognise they are experiencing asthma symptoms often do not adhere to therapies, often due to perceived misunderstandings around medication side-effects, or lack of perceived benefits to using asthma action plans. This analysis provided us with pathways of how a behaviour change intervention might work, focusing on behaviour change concepts recommended in the literature we developed a list of features which a website should have. This list was iteratively modified with input from end users and an expert panel, until a draft of proposed web pages had been developed. These were then gradually converted to working interactive webpages and refined over 10 think aloud studies, to lead to the final website which is being evaluated in the RAISIN trial [23]. Our BCT mapping exercise demonstrates that

| Table 5 Contents of Living Well with Asthma resource |
|---------------------------------|---------------------------------|
| **Topic**                      | **Summary of content**          |
| Introduction pages*            | This section encourages users to recognise whether they are putting up with symptoms unnecessarily, and introduces concepts such as goal setting and its potential benefits. |
| **My Asthma**                  | There are three versions of this section tailored to current use of preventer therapy as chosen by the user: |
| 1) I have never used/been prescribed a preventer |
| 2) I have been prescribed a preventer but don’t really use it |
| 3) I mostly/always take my preventer inhaler as prescribed |
| **Treatments**                 | This section covers adherence and challenges negative beliefs about inhaled steroids. |
| Provides information about different treatments. Links to videos to demonstrate inhaler technique and encourages users to consider whether they are on the correct ‘step’ of the asthma treatment ladder. |
| **Asthma Reviews**             | Promotes attendance at asthma reviews outlining potential benefits to symptoms and quality of life. Prompts user to recognise if putting up with symptoms, and to recognise if they are at risk of asthma attacks. |
| **Action Plans**               | Describes what action plans are and their potential benefits. Provides a template action plan that can also be used by practice nurses during asthma reviews in local health boards. |
| **Physical Activity**          | Promotes benefits of physical activity, and challenges negative beliefs about exercising with asthma. Provides practical advice and tips to encourage users to increase their activity levels. |
| **Common concerns and queries**| Answers 15 common queries and concerns that people with asthma may have, developed from the literature, focus groups and during think aloud studies. For example: I am worried about taking inhaled steroids long term, should I be? Why are some days better than others? |
| **Stress & Anxiety**           | Promotes recognition of the role of stress on asthma, and how having asthma symptoms can lead to stress. Provides suggestions for reducing stress and anxiety. |
| **Take the 4 week Challenge**  | The user is prompted to commit to taking their preventer inhaler regularly for 4 weeks. Users can choose from a list of provided ‘barriers’ to taking their inhalers and review suggested strategies or can free text their own. They may sign up to receive weekly emails during the challenge. |
| **Like to stop smoking?**       | This links to an external website called ‘StopAdvisor’ [19]. This has been developed using LifeGuide software and further details are available elsewhere. |
| **Useful info and links**       | This re-lists information and useful links that have been included elsewhere in the website. |
| **Email reminders**             | These emails are sent every two months. They all include the RCP 3 Questions to encourage the user to assess their current control and prompt them to visit the website or see their nurse or doctor if appropriate. There are also reminders to order inhalers, or other medications (e.g. in time for hay fever season), or if going on holidays. |

*All users are directed through these two sections at first login, and can optionally visit again during future sessions

Discussion

We have demonstrated the feasibility of developing an evidence-based, theory guided, user friendly behaviour change intervention in the form of Living well with Asthma—a website to support self-management in adults with asthma. We have been guided by the MRC Framework on developing and evaluating complex interventions, and as a result directed much effort to the key, yet often overlooked, planning stages [5, 18]. We undertook recommended key tasks to guide our development methods [5], see Table 1, through: synthesis of empirical evidence, using expert knowledge and experience, and incorporating theoretical concepts with end user input, to produce an evidence based behaviour change website. Our evidence synthesis highlighted that self-management of asthma is an underused, yet proven, treatment strategy [7] and that people with asthma frequently do not use therapies optimally, tolerate high levels of symptom burden, and do not attend asthma reviews or make use of asthma action plans. This underestimation of symptoms and overestimation of control is a barrier to making use of available therapies. Those who do recognise they are experiencing asthma symptoms often do not adhere to therapies, often due to perceived misunderstandings around medication side-effects, or lack of perceived benefits to using asthma action plans. This analysis provided us with pathways of how a behaviour change intervention might work, focusing on behaviour change concepts recommended in the literature we developed a list of features which a website should have. This list was iteratively modified with input from end users and an expert panel, until a draft of proposed web pages had been developed. These were then gradually converted to working interactive webpages and refined over 10 think aloud studies, to lead to the final website which is being evaluated in the RAISIN trial [23]. Our BCT mapping exercise demonstrates that
### Table 6: Behaviour change technique mapping of Living Well with Asthma resource

<table>
<thead>
<tr>
<th>No/ Label [21]</th>
<th>Definition</th>
<th>Sections</th>
<th>Example within LWWA website</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Goals and planning</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1 Goal setting (behaviour)</td>
<td>Set or agree on a goal defined in terms of the behaviour to be achieved</td>
<td>4 week challenge</td>
<td>Users commit to taking their preventer inhaler regularly for 4 weeks.</td>
</tr>
<tr>
<td>1.2 Problem solving</td>
<td>Analyse, or prompt the person to analyse, factors influencing the behaviour and generate or select strategies that include overcoming barriers and/or increasing facilitators (includes ‘Relapse Prevention’ and ‘Coping Planning’)</td>
<td>My asthma Concerns &amp; queries 4 week challenge</td>
<td>Users are prompted to consider reasons why they find it difficult to take their inhaler regularly (choosing from a list or free texting own). They are then presented with sample strategies to overcome identified barriers.</td>
</tr>
<tr>
<td>1.3 Goal setting (outcome)</td>
<td>Set or agree on a goal defined in terms of a positive outcome of wanted behaviour</td>
<td>Intro</td>
<td>Users are asked to identify how their asthma can negatively affect their everyday lives. They are then asked to review positive outcome goals to overcome these negative effects.</td>
</tr>
<tr>
<td><strong>Social support</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.6 Discrepancy between current behaviour and goal</td>
<td>Draw attention to discrepancies between a person’s current behaviour (in terms of the form, frequency, duration, or intensity of that behaviour) and the person’s previously set outcome goals, behavioural goals or action plans (goes beyond self-monitoring of behaviour)</td>
<td>Asthma Review</td>
<td>Users are presented with sample strategies to overcome identified barriers.</td>
</tr>
<tr>
<td>1.9 Commitment</td>
<td>Ask the person to affirm or reaffirm statements indicating commitment to change the behaviour Note: if defined in terms of the behaviour to be achieved also code 1.1, Goal setting (behaviour)</td>
<td>4 week challenge</td>
<td>Users tick three statements confirming they are committed to taking their preventer inhaler regularly for the duration of the 4 week challenge.</td>
</tr>
<tr>
<td><strong>Shaping knowledge</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.1 Instruction on how to perform a behavior</td>
<td>Advise on how to perform the behaviour (includes ‘Skills training’)</td>
<td>Treatments Asthma Review Exercise</td>
<td>Users are given step by step instructions on how to use an inhaler correctly. This is followed up by a video demonstration.</td>
</tr>
<tr>
<td>4.3 Re-attribution</td>
<td>Elicit perceived causes of behaviour and suggest alternative explanations (e.g. external or internal and stable or unstable)</td>
<td>Concerns &amp; queries</td>
<td>Describe common reasons why people with asthma put up with symptoms, illustrating that these beliefs are mistaken and providing alternative explanations for the symptoms.</td>
</tr>
<tr>
<td><strong>Natural consequences</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.1 Information about health consequences</td>
<td>Provide information (e.g. written, verbal, visual) about health consequences of performing the behaviour</td>
<td>Intro My asthma Treatments Asthma review Exercise Concerns &amp; queries Action plans</td>
<td>Information provided that people who attend for regular asthma reviews have fewer symptoms and fewer asthma attacks.</td>
</tr>
<tr>
<td>5.3 Information about social and environmental consequences</td>
<td>Provide information (e.g. written, verbal, visual) about social and environmental consequences of performing the behaviour</td>
<td>Asthma review Exercise</td>
<td>Information provided that people who attend for regular asthma reviews have fewer days off school and work, and fewer limitations in activities.</td>
</tr>
<tr>
<td>5.6 Information about emotional consequences</td>
<td>Provide information (e.g. written, verbal, visual) about emotional consequences of performing the behaviour</td>
<td>Concerns &amp; queries</td>
<td>People with asthma describe feeling embarrassed or ashamed taking inhalers in public. Information provided to overcome these concerns and increase confidence about using medications in public.</td>
</tr>
<tr>
<td><strong>Comparison of behaviour</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.1 Demonstration of the behaviour</td>
<td>Provide an observable sample of the performance of the behaviour, directly in person or indirectly e.g. via film, pictures, for the person to aspire to or imitate (includes ‘Modelling’).</td>
<td>My asthma Treatments Asthma review Exercise Action plans</td>
<td>Quotes for adults with asthma demonstrating how their lives changed for the better when they started taking their inhalers regularly.</td>
</tr>
<tr>
<td>6.2 Social comparison</td>
<td>Draw attention to others’ performance to allow comparison with the person’s own performance</td>
<td>My asthma Concerns &amp; queries</td>
<td>In those who have identified that their asthma affects their work they are advised that this is the case with up to 40% of people with asthma.</td>
</tr>
</tbody>
</table>
the resource makes use of multiple BCTs, a strategy which in some health domains has been associated with increased effect sizes [37]. In particular we use goals and planning as a key behavioural technique, which has been shown to be efficacious in asthma [1].

**Strengths**

This study followed recommended processes for developing complex evaluations, and was undertaken by a multidisciplinary team with a range of essential skills, knowledge and experience (including behaviour change theory and implementation theory). A key strength of this resource is in its co-design with potential end users, who had opportunity for input both at the early development planning stages in the form of focus groups, and also towards the end where their input via think aloud studies was invaluable in improving the usability of the resource, in line with the Person Based Approach [15]. The use of LifeGuide software allowed for a streamlined and iterative process of website development where the researcher taking the think aloud studies could modify the website directly following think aloud studies, or from feedback from the expert panel. Most computer programmers do not have a background in healthcare, and therefore removing the need to communicate user feedback to a programmer by using LifeGuide made the process far more efficient.

**Limitations**

In the focus groups we invited both practice nurses and adults with asthma which could be construed as a limitation. However there are advantages to bringing together a diverse group of participants and we felt this was the case here [40]. This can maximise the exploration of different perspectives, which was pertinent here where differences in health professional and patient opinion is a recognised barrier to optimal uptake of self-management practices [31]. The adults with asthma participating in the focus groups and think aloud studies had more severe asthma and were on more treatments than typical primary care patients. This is almost certainly because of them being

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**Table 6** Behaviour change technique mapping of Living Well with Asthma resource (Continued)

<table>
<thead>
<tr>
<th>6.3 Information about others’ approval</th>
<th>Provide information about what other people think about the behaviour. The information clarifies whether others will like, approve or disapprove of what the person is doing or will do</th>
<th>Asthma review</th>
<th>Quote from practice nurse praising people who proactively attend for asthma reviews.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associations</td>
<td>Introduce or define environmental or social stimulus with the purpose of prompting or cueing the behaviour. The prompt or cue would normally occur at the time or place of performance</td>
<td>4 week challenge Emails</td>
<td>Users who sign up to the 4 week challenge are sent weekly emails to remind them of the challenge and prompt them to continue.</td>
</tr>
<tr>
<td>Repetition and substitution</td>
<td>Prompt substitution of the unwanted behaviour with a wanted or neutral behaviour</td>
<td>Exercise</td>
<td>Users are provided with sample strategies to increase their levels of physical activity such as walking to the shops rather than taking the car, or giving up a TV programme for a dance class.</td>
</tr>
<tr>
<td>Repetition and substitution</td>
<td>Prompt rehearsal and repetition of the behaviour in the same context repeatedly so that the context elicits the behaviour</td>
<td>4 week challenge</td>
<td>Strategies for prompting users to remember to take inhalers are suggested such as using them at the same time as teeth brushing or the evening meal.</td>
</tr>
<tr>
<td>Comparison of outcomes</td>
<td>Present verbal or visual communication from a credible source in favour of or against the behaviour</td>
<td>Exercise</td>
<td>Bradley Wiggins quote describing how asthma doesn’t stop him exercising.</td>
</tr>
<tr>
<td>Antecedents</td>
<td>Add objects to the environment in order to facilitate performance of the behaviour.</td>
<td>4 week challenge</td>
<td>Strategies for prompting users to remember to take inhalers are suggested such having an extra inhaler at work, if they regularly forget their morning dose.</td>
</tr>
<tr>
<td>Self-belief</td>
<td>Tell the person that they can successfully perform the wanted behaviour, arguing against self-doubts and asserting that they can and will succeed</td>
<td>Exercise (external video)</td>
<td>Users are directed to a video which promotes the message that anyone regardless of health status and fitness levels can successfully increase their levels of physical activity.</td>
</tr>
</tbody>
</table>
recruited through their participation in asthma advocacy organisations (Asthma UK). We managed this by tempering the suggestions and feedback from these end users with the practical experience of the respiratory physicians and GPs on the expert panel and the practice nurses present in the focus groups. In future studies concentrating recruitment to end users more typical of a primary care population would be worthwhile, although may be difficult.

The same researcher who developed the website, also undertook the think aloud studies. While this had benefits in terms of speed of modifying the resource, we were concerned that participants in the think aloud studies may not have felt comfortable criticising the resource openly in the presence of the person who was also developing it. In order to counter this it was explained that it was easy to make changes with the LifeGuide software and those critical comments were often the most helpful. Exploring the scope of this limitation by counting negative comments was useful, as the high proportion of negative comments or suggestions for improvements suggests that participants did feel comfortable being critical of the website.

Future considerations
The ultimate aim of following the updated MRC guidance on the development and evaluation of complex interventions is to reduce the number of interventions which are developed, but don’t translate into everyday use, and avoiding costly large RCTs which due to unforeseen circumstances are unable to answer the research question posed [18]. The iterative methods of development used here should minimise this risk, and the ongoing RAISIN pilot RCT should allow for meaningful estimates of effect sizes and recruitment and retention rates for any future full scale randomised controlled trial. A qualitative evaluation, involving participant interviews and using NPT to guide analysis, is embedded in the RAISIN trial and will provide rich data on the how the intervention can be improved and its future implementability in the real world [24].

Conclusion
We have developed a resource which our preliminary usability testing suggests is relevant and usable by its target audience. We have outlined the key steps undertaken which included synthesis of knowledge and experience from our expert panel, with a broad exploration of the literature, overarching use of appropriate theory (behaviour change and implementation) and also with input from potential stakeholders (adults with asthma and practice nurses) from an early planning stage. Such methods are rarely fully detailed in the literature and thus the description of this process should be of interest to the growing cadre of researchers developing digital interventions. This paper demonstrates how data from a wide range of sources can directly and practically influence the contents of such a self-management website.

Additional files

Additional file 1: Rationale behind choosing the contents for Living Well with Asthma resource.
Additional file 2: Additional sample screenshots from Living Well with Asthma.

Abbreviations
AAP: Asthma Action Plans; ACQ: Asthma Control Questionnaire; BCT: Behaviour Change Technique; HP: Health Professional; ICT: Information and Communication Technology; IQR: Interquartile Range; ISRCTN: International Standard Randomised Controlled Trial Number; MRC: Medical Research Council; NPT: Normalization Process Theory; PEF: Peak Expiratory Flow; RAISIN: Randomized Trial of an Asthma Internet Self-Management Intervention; RCP 3Q: Royal College of Physicians 3 Questions; RCT: Randomized Controlled Trial; SIMD: Scottish Index of Multiple Deprivation; TA: Think aloud; WP: Work package.

Competing interests
This project (developing and evaluating the Living well with Asthma resource) was funded through a clinical academic fellowship awarded to DM by the Chief Scientist Office, Scottish Government http://www.cso.scot.nhs.uk/ (ref CAF 11/08). The funders played no part in the design, data collection, data analysis/interpretation, the writing of the manuscript; or in the decision to submit the manuscript for publication. All other authors received no direct funding for their role in this project.

MT declares neither he nor any member of his close family has any shares in pharmaceutical companies. In the last 3 years he has received speaker’s honoraria for speaking at sponsored meetings or satellite symposia at conferences from the following companies marketing respiratory and allergy products: Aerocrine, Astra Zeneca, Boehringer Ingleheim, Novartis, GSK, Teva. He has received honoraria for attending advisory panels with: Aerocrine, Almirall, Astra Zeneca, BI, Chiesi, GSK, MSD, Novartis. He has received sponsorship to attend international scientific meetings from: GSK, Astra Zeneca, Mundipharma. He has received funding for research projects from: GSK, Almirall.

All other authors declare that they have no competing interests.

Authors’ contributions
DM planned and developed the website in collaboration with FSM, RC, MML, MT, NCT, LY, SW who were all members of the expert panel. Recruitment of participants was undertaken by DM. Focus groups and think aloud studies undertaken by DM. Analysis of focus group and think aloud transcripts by DM, FM and SW. DM wrote the first draft of the manuscript and refined it based on comments and feedback from all other authors. All authors read and approved the final manuscript.

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References


Appendix 3

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Findings from a pilot Randomised trial of an Asthma Internet Self-management Intervention (RAISIN)

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ABSTRACT

Objective: To evaluate the feasibility of a phase 3 randomised controlled trial (RCT) of a website (Living Well with Asthma) to support self-management.

Design and setting: Phase 2, parallel group, RCT, participants recruited from 20 general practices across Glasgow, UK. Randomisation through automated voice response, after baseline data collection, to website access for minimum 12 weeks or usual care.

Participants: Adults (age ≥16 years) with physician diagnosed, symptomatic asthma (Asthma Control Questionnaire (ACQ) score ≥1). People with unstable asthma or other lung disease were excluded.

Intervention: ‘Living Well with Asthma’ is a desktop/laptop compatible interactive website designed with input from asthma/behaviour change specialists, and adults with asthma. It aims to support optimal medication management, promote use of action plans, encourage attendance at asthma reviews and increase physical activity.

Outcome measures: Primary outcomes were recruitment/retention, website use, ACQ and mini-Asthma Quality of Life Questionnaire (AQLQ). Secondary outcomes included patient activation, prescribing, adherence, spirometry, lung inflammation and health service contacts after 12 weeks. Blinding postrandomisation was not possible.

Results: Recruitment target met. 51 participants randomised (25 intervention group). Age range 16–78 years; 75% female; 28% from most deprived quintile. 45/51 (88%; 20 intervention group) followed postrandomisation was not possible.

Strengths and limitations of this study

- A recent UK review of asthma deaths showed many could have been avoided if medication management and other self-management strategies had been better, so finding optimum approaches to support self-management of asthma is critical and digital interventions show promise.
- The ‘Living Well with Asthma’ website was iteratively designed with input from experts in asthma, self-management support, behaviour change and adults with asthma themselves; it aims to support optimal medication management, promote use of action plans, encourage attendance at asthma reviews and increase physical activity.
- We conducted a phase 2 parallel group, randomised controlled trial: randomisation was through automated voice response, after baseline data collection but blinding of the researchers or participants at outcome, measurement was not possible.
- Our low response rate is a concern; however, we have described our population in detail (unlike previous reports of digital interventions for asthma self-management), and our baseline characteristics demonstrate that patients were recruited from a range of socioeconomic backgrounds.

INTRODUCTION

Asthma is a common condition affecting over 300 million people worldwide, with increasing global prevalence.1 While there are newer pharmacological treatments for individuals with severe asthma,2–5 improvements in outcomes for the majority with mild-to-moderate asthma have stalled.6 A recent UK review of asthma deaths showed potentially avoidable factors in the majority, particularly relating to self-management and adherence to treatment.7 Despite clear evidence that self-management education, asthma action plan
use and regular professional review improve outcomes, translation into everyday practice has proven difficult, and most patients still lack an action plan and sufficient understanding to self-manage effectively. Poor adherence to regular preventative medication (primarily with inhaled corticosteroids, ICS) is a particular problem. Using digital interventions to promote self-management behaviours shows promise, but uncertainty persists as to the most effective formulation of the intervention and the target population.9

In this phase 2, pilot randomised controlled trial (RCT), we evaluated the feasibility and effectiveness of using a low-intensity online intervention aimed at promoting effective self-management (especially adherence to ICS) in adults with mild-to-moderate asthma, compared with usual care. We developed the intervention (‘Living Well with Asthma’) incorporating evidence from the literature and relevant theory. Several phases of user testing in alignment with the ‘person-based approach’ to developing digital behaviour change interventions were undertaken.10 Following the Medical Research Council (MRC) guidance on developing and evaluating complex interventions,11 our objective was to determine the feasibility of conducting a phase 3 RCT, and obtained initial estimates of effects on outcomes.

**METHODS**

Our trial protocol is described in detail elsewhere.12 A brief summary is provided here.

**Settings and participants**

We recruited from 20 general practices in Glasgow, UK, between 23/09/2013 and 21/02/2014, using clinical databases to identify potential participants who were invited by mail to participate and complete the Asthma Control Questionnaire (ACQ). We recruited adults aged 16 years or older, with a physician diagnosis of asthma and ACQ score ≥1, who provided written informed consent. For full inclusion and exclusion criteria see box 1. Our search strategy is shown in the online supplementary data file.

**Study design overview and intervention description**

We conducted a non-blinded pilot RCT of access to the ‘Living Well with Asthma’ website versus usual care for 51 participants. Participants were assessed in their own homes at baseline and at 12 weeks or as soon as possible after this date.

The intervention development is described elsewhere,13 but in summary aimed to (1) provide understanding of current level of asthma control and how to improve it, specifically by optimising use of prescribed medication; (2) challenge attitudes and concerns around medications; (3) learn how to get the most out of their annual asthma review; (4) prompt provision and use of a personal asthma action plan from a health professional and (5) send timely reminders for influenza vaccination and reordering refill inhaler prescriptions. The website did not advise medication changes, but suggested contacting a health professional if inadequate control was identified, with clear advice for seeking help in an emergency. The website is interactive, aiming to engage the user in recognising that their asthma is uncontrolled, and illustrate the benefits via case vignettes (based on real life examples) of taking their medications as prescribed. The website is tailored based on their current use of preventer inhalers (never been prescribed; prescribed but do not really use; use regularly). There is a ‘4-week challenge’ that users can sign up to, where they commit to taking their preventer regularly for 4 weeks, are guided through establishing their personal barriers to regular use (see screenshot in online supplementary data file for further illustration) and developing potential solutions to these barriers.

The intervention group was given website login details and a computer link, and advised to use the website as much or as little as they wished (total time to visit all pages once ∼90 min). We developed the website using an open source software package called LifeGuide.14 15

**Randomisation and blinding**

Randomisation occurred after baseline data collection, using a third party interactive voice response system (IVRS) ensuring allocation concealment. The randomisation schedule was generated in advance of the study by the Robertson Centre for Biostatistics, in a 1:1 ratio, using the method of randomised permuted blocks of length 4, without stratification. Access to the
randomisation schedule was restricted to those within the Centre with responsibility for provision of the IVRS. The comparison group was offered access to the intervention after the follow-up visit.

**Primary outcomes**
The primary end points were: recruitment and retention rates at follow-up, website use, and changes from baseline for ACQ\(^{16}\) and mini-Asthma Quality of Life Questionnaire (AQLQ) scores.\(^{17}\) The ACQ and mini-AQLQ have a minimal clinically important difference (MCID) of 0.5.\(^{19}\) This pilot study was not powered to detect a difference in these two clinical outcomes; they were included in order to assess feasibility and inform sample size calculations for a future full-scale RCT.

**Secondary outcomes**
We evaluated a range of secondary outcomes in order to assess their feasibility for use in a future full-scale RCT.

Individual domains of the mini-AQLQ were reported. These comprise of symptoms, activity limitation, emotional function and environmental stimuli. Knowledge, skills and confidence to manage health was measured via the Patient Activation Measure (PAM).\(^{19}\) Self-reported adherence was assessed by both enquiring what proportion of prescribed ICS were actually taken, and via the Morisky Medication Adherence Scale (MMAS).\(^{20}\) Airway inflammation is measured by fraction exhaled nitric oxide (FeNO).\(^{21}\) Lung function was assessed via prebronchodilator spirometry, including forced expiratory volume in 1 s (FEV\(_1\)); FEV\(_1\) percentage predicted; and FEV\(_1\)/forced vital capacity. Lung function (spirometry) was performed to the American Thoracic Society (ATS) standards,\(^{21}\)\(^{22}\) where possible, and the proportion of tests not meeting these standards recorded. As well as the asthma-specific mini-AQLQ, generic quality of life was measured using the EuroQol (EQ)-5D.\(^{25}\) We collected changes to medication use, recorded numbers of health service contacts and severe exacerbations were noted by recording the number of oral prednisolone courses. These data were self-reported. Those in the intervention group received the problematic experience of therapies scale (PETS) to facilitate understandings of barriers to using the website, and following its advice.

**Data analysis**
Continuous data are summarised as mean and SD or range, or as median and IQR, and categorical data as counts and percentages. Linear regression was used to estimate differences in continuous outcomes between groups at follow-up, adjusting for baseline scores. Estimated between-group differences are reported with a 95% CI and p value. For continuous outcomes that were not normally distributed, changes from baseline were compared between groups using Wilcoxon rank-sum tests. Categorical variables were compared between groups using Fisher’s exact test. All analyses were carried out using SPSS Statistics V22 and Microsoft Office Excel. The primary analysis was intention-to-treat and involved all patients who were randomly assigned, except with spirometry where only those meeting ATS/European Respiratory Society (ERS) eligibility criteria will be analysed.\(^{22}\)

**RESULTS**

**Baseline characteristics**
The groups were largely well matched. Participants were aged between 16 and 78 years, and 75% were female (table 1).

**Primary outcomes**

**Recruitment and retention**
Recruitment target of 50 participants was met (figure 1). Participating practices were mostly urban, and spread across deprivation categories. Response rate to the postal invitation was 4.6%, lower than anticipated, and only 27% of those screened were subsequently randomised, with the majority failing due to ACQ<1 (75%). Those randomised were younger (45.5 vs 51.5 years) and more likely to be female (75% vs 50%) than screen failures, but with similar socioeconomic deprivation. The attrition rate (not completing follow-up) was 12%: 20% in the intervention group, 4% in the comparison group (Fisher’s test p=0.10).

**Website use**
Nineteen of the 25 participants in the intervention group logged in at least once (76%) with 17 going beyond the initial ‘core’ section. The subsequent section was tailored depending on which of three options was chosen: (1) I have never been prescribed a preventer inhaler (n=1); (2) I have been prescribed an inhaler but do not really use it (n=6); or (3) I have a preventer and usually use it as prescribed (n=10). The mean number of logins was 1.8 (range 0–7), median 1, (IQR 1–2), and the average time spent on the website during the study period was 18 min (range 0–48.9). More detail is shown in online supplementary figure A.

Beyond the core ‘introduction’ and ‘my asthma’ sections, the most popular sections were ‘take the 4-week challenge’ (n=13), and ‘common concerns and queries’ (n=11). Further usage data are shown in online supplementary table B. The majority (95%) of participants acknowledged that asthma was impacting on their life (online supplementary table C).

**ACQ score**
Our planned analysis was for the seven-question version of the ACQ, which includes spirometry, for which there was considerable missing data (n=23; table 1). There was no significant difference in the intervention group compared with the control group (−0.42 (95% CI −0.95 to 0.11), p=0.121). We also analysed the equally valid six-question version (without spirometry)\(^{24}\) which was
available for all (n=45), and demonstrated a similar result and it is this result which is presented in table 2.

Fifty-five per cent of the intervention group and 48% of the comparison group achieved the MCID of an improvement of at least 0.5 points (p=0.767).

AQLQ score
There was no significant difference in mini-AQLQ scores in the intervention group compared with the control group (table 2). Fifty per cent of the intervention group and 36% in the comparison group achieved the MCID of improvement of at least 0.5 points (p=0.379).

Secondary outcomes
The rationale for including a range of secondary outcomes was to assess their feasibility for inclusion in any future full-scale RCT. All outcomes were acceptable to participants and feasible to measure and analyse, apart from spirometry.

Mini-AQLQ domain scores
The ‘activity limitation’ domain of the mini-AQLQ showed a statistically significant improvement in scores in favour of the intervention group (table 3). The remaining individual domains of the mini-AQLQ showed numerical improvement in the intervention group, which were not statistically significant.

Other patient-centred outcomes
There was a significant improvement in PAM scores (tables 3 and 4) in the intervention group compared with the control group, indicating that intervention patients were more highly activated in relation to managing their own health.

There was no significant difference in mean MMAS scores in the intervention group (table 3) compared with the control group. However, more participants in the intervention group achieved the MCID≥2 compared with usual care (30% vs 4%, p=0.034), although the intervention group did have lower baseline scores.

The change in EQ-5D health utility score showed no significant between-group difference (table 4), with median change in score of 0 in both groups.

Physiological and inflammatory outcomes
Spirometry analysis included only those meeting ATS acceptability standards (22/45, 11 per group). Effect sizes were small, and none achieved statistical significance (table 3).

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Table 1  Baseline demographic characteristics of study population per group

<table>
<thead>
<tr>
<th></th>
<th>Overall (n=51)</th>
<th>Comparison (n=26)</th>
<th>Intervention (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean (SD)</td>
<td>45.5 (15)</td>
<td>46.4 (14)</td>
<td>44.6 (17)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>38 (75)</td>
<td>20 (77)</td>
<td>18 (72)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White, n (%)</td>
<td>48 (94)</td>
<td>24 (92)</td>
<td>24 (96)</td>
</tr>
<tr>
<td>Other, n (%)</td>
<td>3 (6)</td>
<td>2 (8)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Smoking status:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current, n (%)</td>
<td>5 (10)</td>
<td>2 (8)</td>
<td>3 (12)</td>
</tr>
<tr>
<td>Former smoker, n (%)</td>
<td>18 (35)</td>
<td>11 (42)</td>
<td>7 (28)</td>
</tr>
<tr>
<td>Never smoked, n (%)</td>
<td>28 (55)</td>
<td>13 (50)</td>
<td>15 (60)</td>
</tr>
<tr>
<td>SIMD quintile (1=most deprived, 5=least deprived)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIMD 1, n (%)</td>
<td>14 (28)</td>
<td>7 (27)</td>
<td>7 (28)</td>
</tr>
<tr>
<td>SIMD 2, n (%)</td>
<td>11 (22)</td>
<td>6 (23)</td>
<td>5 (20)</td>
</tr>
<tr>
<td>SIMD 3, n (%)</td>
<td>9 (18)</td>
<td>4 (15)</td>
<td>5 (20)</td>
</tr>
<tr>
<td>SIMD 4, n (%)</td>
<td>5 (10)</td>
<td>3 (12)</td>
<td>2 (8)</td>
</tr>
<tr>
<td>SIMD 5, n (%)</td>
<td>12 (24)</td>
<td>6 (23)</td>
<td>6 (24)</td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed, n (%)</td>
<td>25 (49)</td>
<td>11 (42)</td>
<td>14 (56)</td>
</tr>
<tr>
<td>Unemployed, n (%)</td>
<td>8 (16)</td>
<td>3 (12)</td>
<td>5 (20)</td>
</tr>
<tr>
<td>Retired, n (%)</td>
<td>9 (18)</td>
<td>5 (19)</td>
<td>4 (16)</td>
</tr>
<tr>
<td>Student, n (%)</td>
<td>2 (4)</td>
<td>1 (4)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Other, n (%)</td>
<td>7 (14)</td>
<td>6 (23)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary education, n (%)</td>
<td>18 (35)</td>
<td>7 (27)</td>
<td>11 (44)</td>
</tr>
<tr>
<td>Tertiary/further education, n (%)</td>
<td>33 (65)</td>
<td>19 (73)</td>
<td>14 (56)</td>
</tr>
<tr>
<td>BMI (kg/m²), mean(SD)</td>
<td>30.4 (6.8)</td>
<td>31.3 (8.0)</td>
<td>29.4 (5.2)</td>
</tr>
<tr>
<td>Number of comorbidities (over and above index condition), mean (SD)</td>
<td>2.6 (1.7)</td>
<td>2.6 (1.9)</td>
<td>2.6 (1.4)</td>
</tr>
<tr>
<td>Length of asthma diagnosis (years), median (IQR)</td>
<td>18.5 (8.6–28.6)</td>
<td>17.0 (8.6–27.8)</td>
<td>20.3 (9.7–28.6)</td>
</tr>
</tbody>
</table>

BMI, body mass index; SIMD, Scottish Index of Multiple Deprivation.
**Figure 1** Flow of participants through study. *Actual search terms refined iteratively through recruitment (see online supplementary data file for detail). ACQ, Asthma Control Questionnaire score; FeNO, fractional exhaled nitric oxide; NHS, National Health Service.

**Table 2** Primary outcomes (ACQ and mini-AQLQ)

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
<th>Estimated difference (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACQ score 6-question version (continuous 0–6; 0=totally controlled, 6=severely uncontrolled)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Mean (SD)</td>
<td>1.87 (0.59)</td>
<td>1.97 (0.68)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up Mean (SD)</td>
<td>1.22 (0.91)</td>
<td>1.65 (1.15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change Mean (SD)</td>
<td>−0.65 (1.08)</td>
<td>−0.32 (0.94)</td>
<td>−0.36 (−0.96 to 0.23)</td>
<td>0.225</td>
</tr>
<tr>
<td>ACQ score 6-question version (MCID improvement at follow-up)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improvement ≥0.5 n (%)</td>
<td>11 (55%)</td>
<td>12 (48%)</td>
<td></td>
<td>0.767</td>
</tr>
<tr>
<td>Mini-AQLQ score (continuous 1–7; 1=severely impaired; 7=not impaired at all)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Mean (SD)</td>
<td>4.97 (1.03)</td>
<td>4.65 (1.02)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up Mean (SD)</td>
<td>5.40 (1.01)</td>
<td>4.76 (1.30)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change Mean (SD)</td>
<td>0.43 (0.78)</td>
<td>0.11 (0.88)</td>
<td>0.38 (−0.13 to 0.89)</td>
<td>0.136</td>
</tr>
<tr>
<td>Mini-AQLQ score (MCID improvement at follow-up)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improvement ≥0.5 n (%)</td>
<td>10 (50%)</td>
<td>9 (36%)</td>
<td></td>
<td>0.379</td>
</tr>
</tbody>
</table>

Summaries of scores at baseline, follow-up and change from baseline, with estimated between-group difference from baseline-adjusted linear regression model with 95% CI and p value. Summaries of achievement of an improvement by more than the MCID at follow-up, with Fisher’s exact test p values to compare groups.

ACQ, Asthma Control Questionnaire (fall in score is desirable); AQLQ, Asthma Quality of Life Questionnaire (rise in score desirable); MCID, minimum clinically important difference.
FeNO levels (indicating airways eosinophilic inflammation) showed no significant between-group difference (table 4).

Medication changes and health service contacts
The median weekly number of puffs of reliever inhaler used in the intervention group reduced from 11 to 5, but remained unchanged in the control group at 4 puffs per week at baseline and at follow-up (p=0.022) (table 4). Although this between-group change in bronchodilator use was statistically significant, the groups were imbalanced at baseline. There was no significant between-group difference in the percentage of recommended ICS doses self-reportedly taken, nor the equivalent beclomethasone doses prescribed. There were no significant between-group differences in health service contacts or prednisolone courses prescribed.

Further feasibility outcomes
The PETS results are shown in online supplementary table A, illustrating barriers to using the website. The biggest barriers relate to time and opportunity, rather than content.

No serious adverse events were recorded.

Table 3 Secondary outcomes (continuous variables normally distributed)

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
<th>Estimated difference (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mini-AQLQ symptom domain score (continuous, 1=severely impaired; 7=not impaired at all)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Mean (SD)</td>
<td>4.56 (1.10)</td>
<td>4.30 (0.84)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up Mean (SD)</td>
<td>5.15 (1.20)</td>
<td>4.38 (1.35)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change Mean (SD)</td>
<td>0.59 (1.10)</td>
<td>0.08 (1.05)</td>
<td>0.56 (−0.08 to 1.22)</td>
<td>0.084</td>
</tr>
<tr>
<td>Mini-AQLQ activity limitation domain score (continuous, 1=severely impaired; 7=not impaired at all)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Mean (SD)</td>
<td>5.30 (1.24)</td>
<td>5.31 (1.33)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up Mean (SD)</td>
<td>5.98 (0.92)</td>
<td>5.38 (1.33)</td>
<td></td>
<td></td>
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<tr>
<td>Change Mean (SD)</td>
<td>0.68 (1.01)</td>
<td>0.07 (1.10)</td>
<td>0.60 (0.05 to 1.15)</td>
<td>0.034</td>
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<tr>
<td>Mini-AQLQ emotional function domain score (continuous, 1=severely impaired; 7=not impaired at all)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Mean (SD)</td>
<td>5.48 (1.09)</td>
<td>4.80 (1.48)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up Mean (SD)</td>
<td>5.75 (1.01)</td>
<td>4.84 (1.82)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change Mean (SD)</td>
<td>0.27 (0.78)</td>
<td>0.04 (1.30)</td>
<td>0.35 (−0.33 to 1.03)</td>
<td>0.301</td>
</tr>
<tr>
<td>Mini-AQLQ environmental domain score (continuous, 1=severely impaired; 7=not impaired at all)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Mean (SD)</td>
<td>4.75 (1.39)</td>
<td>4.11 (1.54)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up Mean (SD)</td>
<td>4.85 (1.30)</td>
<td>4.23 (1.67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change Mean (SD)</td>
<td>0.10 (0.89)</td>
<td>0.12 (0.90)</td>
<td>0.08 (−0.46 to 0.62)</td>
<td>0.768</td>
</tr>
<tr>
<td>PAM (continuous, 0=no activation; 100=high activation)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Mean (SD)</td>
<td>65.7 (10.0)</td>
<td>66.2 (14.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up Mean (SD)</td>
<td>73.0 (13.9)</td>
<td>65.7 (16.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change Mean (SD)</td>
<td>7.3 (11.3)</td>
<td>−0.5 (12.5)</td>
<td>7.72 (0.53 to 14.90)</td>
<td>0.036</td>
</tr>
<tr>
<td>MMAS (continuous, range 0–8, 0=low adherence; 8=high adherence)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Mean (SD)</td>
<td>4.88 (1.97)</td>
<td>5.59 (1.85)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up Mean (SD)</td>
<td>5.46 (1.80)</td>
<td>5.82 (1.85)</td>
<td></td>
<td></td>
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<tr>
<td>Change Mean (SD)</td>
<td>0.58 (1.37)</td>
<td>0.23 (1.03)</td>
<td>0.19 (−0.50 to 0.88)</td>
<td>0.586</td>
</tr>
<tr>
<td>MMAS (MCID improvement at follow-up) Improvement ≥2.0 n (%)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improvement ≥2.0 n (%)</td>
<td>6 (30)</td>
<td>1 (4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1 (L) (continuous) (n=22)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Mean (SD)</td>
<td>2.62 (0.56)</td>
<td>2.66 (0.69)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up Mean (SD)</td>
<td>2.72 (0.58)</td>
<td>2.68 (0.49)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change Mean (SD)</td>
<td>0.10 (0.18)</td>
<td>0.02 (0.31)</td>
<td>0.08 (−0.12 to 0.27)</td>
<td>0.428</td>
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<tr>
<td>FEV1% predicted (continuous) (n=22)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Baseline Mean (SD)</td>
<td>87.4 (13.6)</td>
<td>85.2 (17.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up Mean (SD)</td>
<td>90.6 (13.8)</td>
<td>85.7 (11.8)</td>
<td></td>
<td></td>
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<tr>
<td>Change Mean (SD)</td>
<td>3.3 (6.3)</td>
<td>0.6 (9.4)</td>
<td>3.4 (−2.8 to 9.5)</td>
<td>0.265</td>
</tr>
<tr>
<td>FEV1/FVC (%) (continuous) (n=22)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Mean (SD)</td>
<td>76.7 (7.0)</td>
<td>77.6 (10.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up Mean (SD)</td>
<td>79.1 (6.7)</td>
<td>80.2 (9.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change Mean (SD)</td>
<td>2.4 (5.3)</td>
<td>2.6 (4.5)</td>
<td>−0.4 (−3.9 to 3.1)</td>
<td>0.829</td>
</tr>
</tbody>
</table>

Summaries of scores at baseline, follow-up and change from baseline, with estimated between-group difference from baseline-adjusted linear regression model with 95% CI and p value. Summaries of achievement of an improvement by more than the MCID at follow-up, with Fisher’s exact test p values to compare groups. N=45 unless otherwise stated. p Values in bold indicate significance <0.05. ACQ, Asthma Control Questionnaire; AQLQ, Asthma Quality of Life Questionnaire; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; MCID, minimum clinically important difference; MMAS, Morisky Medication Adherence Score; PAM, Patient Activation Measure.

FeNO levels (indicating airways eosinophilic inflammation) showed no significant between-group difference (table 4).

Further feasibility outcomes
The PETS results are shown in online supplementary table A, illustrating barriers to using the website. The biggest barriers relate to time and opportunity, rather than content.

No serious adverse events were recorded.
The main source of missing data was from the spirometry results where 23 participants had results not suitable for analysis, due to not meeting ATS criteria. All questionnaires were completed sufficiently well to allow calculation of scores, with only one response missing from each of the mini-AQLQ, PAM and MMAS all from different participants.

Sample size for a fully powered subsequent study

Using baseline-adjusted calculations of the change in ACQ score above assuming a SD of 1.0, a sample size of 134 would be required to detect a between-group change of ≥0.5 (MCID) in ACQ with 90% power at 0.05 significance. Assuming a similar attrition rate of 12%, the total sample size required would be 154.

DISCUSSION

Principal findings

This phase 2 pilot RCT of the Living well with Asthma resource demonstrates that this website merits further development, and that subsequent progression to a full-scale phase 3 RCT is feasible. Recruitment targets were achieved, and attrition rates were comparable to rates of other published digital interventions. We had no upper age limit, unlike similar asthma digital intervention studies. This is important as our recent metareview only found one study that included participants over 50 years of age, and descriptions of participants’ characteristics were limited, with socioeconomic status ignored. This information is important to understand the ‘reach’ of the intervention.

In terms of primary efficacy outcomes, there were no significant between-group differences in terms of ACQ and mini-AQLQ, although it is important to note that this pilot trial was not powered to show such differences. However, there are some interesting findings in analysis, as both the ACQ and mini-AQLQ demonstrate encouraging and consistent trends in favour of the intervention group, with one subdomain of the AQLQ (activity limitation) reaching the MCID and statistical significance. It is worth noting that for both primary efficacy outcomes, a proportion of those in the comparison group demonstrated an improvement in MCID scores as well as the
intervention group. This is often the case in unblinded complex intervention trials, and validates our approach of making this a pilot RCT, and not just a feasibility study. In terms of website use, 76% of individuals logging in is comparable with other behaviour change websites. and it is encouraging that an average of only 18 min usage resulted in consistently positive trends across almost all outcomes. Asthma-specific research indicates that users like to spend 5–8 min per online session. Our exploration of usage patterns suggests that some users missed sections that they could potentially have benefited from. These two facts combined lead us to conclude that it would be preferable to provide the core modules initially and then “release” further sections weekly or fortnightly, a strategy that has been used successfully for a weight loss intervention also developed using LifeGuide software. Qualitative process evaluation interviews of those in the intervention group have been completed and will be reported separately. Findings from this qualitative work will inform the further development of this resource, prior to evaluation in a full-scale trial.

We assessed the feasibility of collecting a range of secondary outcomes in any future RCT, and in doing so demonstrated a significant improvement in the PAM, which indicates that those in the intervention group had improved knowledge, confidence and skills to manage their asthma. Significant between-group differences in the numbers of patients showing a MCID improvement in adherence and reliever use should be interpreted with caution due to baseline between-group imbalances. The feasibility of researchers undertaking spirometry in the participants’ own homes using a portable handheld device was found to be low, as reported in other studies. Potential solutions include more intensive training of research staff; use of a device providing test-by-test acceptability information or undertaking trial visits in a dedicated clinical research facility by staff experienced in spirometry. However, this latter solution could have a negative effect on recruitment, as 21% of our study visits were undertaken in the evening and weekend, which facilitated recruitment of a population who can rarely make it into such RCTs (full-time employed). There is a balance between precision of measurements versus encouraging a more representative sample. Whether spirometry is required at all in a study aimed at people with mild-to-moderate asthma is not clear, and there is precedence in the literature for not including these outcome measures in similar primary care-based trials or for using simpler to perform lung function measures such as peak expiratory flow rate. Lack of time and opportunity were the biggest barriers to using the website and providing the contents on a smartphone app or tablet would be worth investigating. During the introduction questions at the start of the website, 95% of users agreed to statements which showed that asthma was negatively impacting on their lives. However, at the end of the trial, 42% of users doubted the personal relevance of the website, anecdotally reporting that the website would be more useful for people with symptomatic asthma. To be in the trial in the first place, all users were symptomatic (as defined by ACQ score), so challenging this mismatch between users’ perceptions and the reality would be warranted in future versions of a mobile friendly digital intervention.

Strengths and limitations
Blinding to group allocation during analysis was not possible due to the different numbers in each group being known by the researcher undertaking the analysis. As with many digital interventions, the ‘reach’ is a potential issue and our low response rate is a concern, even taking into account our very broad recruitment strategy. Similar trials have described similar recruitment difficulties. However, given how common asthma is, improvements in even a small proportion of patients could lead to significant benefit overall, particularly with an intervention such as that trialled here which is entirely internet-based and once developed is very economical to make available to large numbers of people. Therefore, what seems like a low reach can still improve outcomes for a large number of people. We have described our population in detail, and our baseline characteristics demonstrate that patients were recruited from a range of socioeconomic backgrounds. Those excluded due to not having internet access were older than those who were excluded for other reasons (data not shown), but this is becoming less of an issue with year-on-year increases in the number of households with internet access (84% in 2014, UK). Comparable studies in the literature
Our recently published metareview suggests digital interactive interventions to support asthma self-management show promise, but there is no clear picture about the ‘active ingredients’ of the interventions. In the development of this intervention, we have described its contents fully including an analysis of behaviour change techniques used, allowing more meaningful future comparisons. When focusing on interventions aimed at those with mild-to-moderate asthma, most have included considerable health professional input as well as self-monitoring work on the part of the participants, and have not shown clinical improvements. This evaluation of Living Well with Asthma adds to the literature on digital asthma self-management suggesting that an intervention not including regular user self-monitoring or costly health professional input may have positive results.

Future research
We have shown that evaluating the Living Well with Asthma intervention was feasible and resulted in encouraging trends in clinical outcomes. Further qualitative work to understand usage patterns with intervention...
group participants have been completed and will inform a future version of the resource. To overcome the ‘practical barriers’ to using the intervention, future versions need to be mobile and tablet compatible, and will require further user testing. Following this development work on the resource, these findings suggest that a large-scale phase 3 RCT is merited, with some exploration of recruitment strategies and minor modification to outcome measurement methods. Low-intensity digital interventions that are easier to deliver at scale may be a more successful strategy, particularly in those with mild-to-moderate asthma.

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Contributors DM, FSM and SW led planning and development of the intervention with support from NCT, RC, LY and MT. DM, FSM, SW and AM planned the evaluation, with support from NCT, RC, KA, LY and MT. DM and KS were responsible for recruitment, and DM, KS and KA undertook data collection. DM led data analysis and interpretation with support from FSM, SW, AM, NCT, RC, KS and KA. DM drafted the manuscript with initial support from FSM, SW and AM and additional input from MT, LY, NCT, RC, KS and KA. All authors critically reviewed the manuscript, contributing important intellectual content, and approved the final manuscript.

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Competing interests This project (developing and evaluating the Living well with Asthma resource) was funded through a clinical academic fellowship awarded to DM by the Chief Scientist Office, Scottish Government http://www.cso.scot.nhs.uk/ (ref CAF 11/08). MT declares neither he nor any member of his close family has any shares in pharmaceutical companies. In the past 3 years he has received speaker’s honoraria for speaking at sponsored meetings or satellite symposia at conferences from the following companies marketing respiratory and allergy products: Aerocline, Astra Zeneca, Boehringer Ingleheim, Novartis, GSK, Teva. He has received honoraria for attending advisory panels with; Aerocline, Almirall, Astra Zeneca, Bi, Chiesi, GSK, MSD, Novartis. He has received sponsorship to attend international scientific meetings from: GSK, Astra Zeneca, Mundipharma. He has received funding for research projects from: GSK, Almirall.

Ethics approval This study was approved by the West of Scotland Research Ethics Committee (ref 13/WOS/0004).

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

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Asthma Internet Self-management
Findings from a pilot Randomised trial of an

D Morrison, S Wyke, K Sauderson, A McConnachie, K Agur, R Chaudhuri, M Thomas, N C Thomson, L Yardley and F S Mair

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Appendix 4 Meta-review Protocol

Title: A Qualitative and Quantitative Systematic Review of Reviews of the Use of Online/Web-based/Computerised Asthma Self-care Interventions.

Deborah Morrison, Karolina Agur, Neil Thomson, Sally Wyke, Alex McConnachie, Frances Mair

Review question

What is known about the evidence that web-based/online/computerised tools for self management of asthma can improve indices of asthma control, lung function, health care utilisation, patient quality of life, and patient satisfaction, and what helps or hinders the use of such interventions by patients, carers and health professionals.

Objectives

- To undertake a systematic review of all published reviews (quantitative and qualitative) of web-based/online/computerised self-management asthma interventions.
- To establish if the use of web-based/online/computerised self care interventions have been found to have a positive effect on asthma symptom scores, lung function, medication use, health care utilisation, or asthma quality of life scores.
- To identify the presence of techniques in these interventions known to promote behavioural change e.g. educational information, self monitoring, attitudinal arguments, and the use of prompts.
- To examine what factors, if any, have been identified as promoting or inhibiting the uptake and utilisation of online tools by patients, carers and practitioners?

Searches

- Databases to be searched: MEDLINE, EMBASE, CINAHL, PsycINFO, ERIC, Cochrane Library (including CDSR, DARE, Central, and HTA databases), DoPHER and TROPHI (both produced by the EPPI Centre), Social Science Citation Index and Science Citation Index. These databases will be searched using a combination of subject headings where available (such as MeSH) and words in the title and abstracts.

The search strategy combines 3 facets of search terms:

1. Online technology
2. Asthma
3. Self management/behavior change/patient experience

Searches employing more general terms, such as respiratory tract diseases, will be explored as they may identify records where in the full document it becomes clear that patients with asthma are included.

To minimise the risk of missing relevant reviews a manual search of key resources and journals and of the reference lists of reviews captured by initial searches will be undertaken. The search can also be complemented by contacting experts in the topic under review and by carrying out citation searches for articles which cite individual studies that are known to be relevant to the topic.

Types of study to be included/excluded

Included:

Reviews (qualitative and quantitative) describing the use of online/web-based/computerised decision support software interventions providing education and advice on managing asthma for
patients with asthma, or their carers. Quantitative reviews which describe RCTs, and qualitative reviews which seek to understand the patients or providers’ experience of using these asthma interventions, and those which describe the theory behind the development of such interventions.

Excluded:

- Studies examining clinical decision support software for health professionals.
- Where a review features online/computerised asthma interventions, but the results are indistinguishable from non asthma interventions, or non online/computerised interventions, these papers will be excluded.
- Conference proceedings and theses are excluded.

**Condition or domain being studied**

Asthma is common, and Scotland has the highest prevalence of asthma symptoms in the world, with patients accepting higher levels of symptoms and lifestyle limitations than they need to, often as a result of not making full use of proven treatment strategies. The promotion of self-care is a strategy known to improve asthma control, and the use of mediums such as the internet and mobile phones are increasingly being considered as a tool to augment its use.

This systematic review of reviews will deliver a position paper on the current knowledge regarding the use of online/web-based/computerised asthma self management tools, and identify gaps in the literature.

**Participants/ population**

Quantitative and qualitative studies from any geographical location, participants diagnosed with asthma; being treated in any setting: primary; secondary; tertiary care, e.g. in the hospital, community, home; describing a review of online/web-based/computerised asthma interventions.

**Intervention(s), exposure(s)**

Any review describing the use of online/web-based/computerised asthma interventions to facilitate patients to manage their asthma.

We considered any digital mode of delivery so long as the intervention itself was providing some degree of information or feedback. It needed to be more than telemonitoring, i.e more than a method of communication between users and health professionals. For example a computer programme that collected symptoms or peak flow data to allow a health professional to provide feedback would be excluded.

**Comparator(s)/ control**

Any comparison with usual care, or alternative modes of delivery of selfmanagement information/skills to participants with asthma or their carers.

**Outcome(s)**

**Primary outcomes may include:**

- Measures of asthma control, Symptoms (e.g. diary card scores)
- Measures of asthma quality of life
- Exacerbations
- Restricted activities (e.g. days of work/school/disturbed nights)
- Lung function: e.g. spirometry & reversibility, peak expiratory flow
- Medication utilisation –
 relief inhaled β agonist use
 • Compliance with medication
 • Health service utilisation (including scheduled/unscheduled, and primary/secondary care)
 • Biomarkers of airway inflammation (e.g. exhaled nitric oxide)
 • Facilitators of online asthma intervention use by patients and practitioners
 • Barriers to online asthma intervention use by patients and practitioners
 • Adverse events

Secondary outcomes may include
 • What behavioural change theories are used, if any, to inform online asthma interventions
 • Patient satisfaction
 • Patient knowledge
 • Adherence to monitoring tools
 • Recruitment Retention rates
 • Markers of self care (action plan use, inhaler technique for example)
 • Data about economic benefits

Study Design - Include review papers only.

Definition of a review

We considered a review paper to be one that provides an analytic account of the research literature related to a specific topic or closely related set of topics. It is intended to contribute to knowledge by answering a research question. Thus we include the following types of papers:

1. Systematic reviews: where relevant literature has been identified by means of a structured search of bibliographic and other databases; where transparent methodological criteria are used to exclude papers that do not meet an explicit methodological benchmark, and which presents rigorous conclusions about outcomes.
2. Narrative reviews: where relevant literature has been purposively sampled from a field of research; where theoretical or topical criteria are used to include papers on the grounds of type, relevance, and perceived significance; with the aim of summarising, discussing, and critiquing conclusions.
3. Qualitative metasyntheses or meta-ethnographies, where relevant literature has been identified by means of a structured search of bibliographic and other databases, where transparent methods had been used to draw together theoretical products, with the aim of elaborating and extending theory.

We excluded the following:

1. Secondary analyses (including qualitative metasyntheses or metaethnographies) of existing data-sets for the purposes of presenting cumulative outcomes from personal research programmes.
2. Secondary analyses (including qualitative metasyntheses or metaethnographies) of existing data-sets for the purposes of presenting integrative outcomes from different research programmes.
3. Discussions of literature included in contributions to theory building or critique.
4. Summaries of literature for the purposes of information or commentary.
5. Editorial discussions that argue the case for a field of research or a course of action.
Where the abstract states it is a review, but there is no supporting evidence in the main paper, such as details of databases searched or criteria for selection of papers (either on methodological or theoretical grounds), the paper is excluded.

**Data extraction, (selection and coding)**

Title, abstract and full paper screening will be carried out by two researchers independently using Distiller software. The full text of the potentially relevant studies will be retrieved and assessed independently for inclusion as per criteria mentioned. Excluded studies will be listed with reasons of exclusion. Data extraction and data analysis will be carried out using a combination of Distiller software, NVivo software and Microsoft Word. Any disagreements will be resolved by discussion, with a third party if necessary.

**Risk of bias (quality) assessment**

The AMSTAR tool has been validated as a means to assess the methodological quality of systematic reviews included, and will be utilised during the quality appraisal of included studies [1]. Those achieving 50% plus a ‘yes’ to question 7 will be included, with appropriate concessions for qualitative studies.

**Strategy for data synthesis**

Numerical data, e.g. the total number of participants will be analysed using descriptive statistics. Outcomes from the quantitative reviews will be analysed using appropriate statistical methods. Clinical and methodological heterogeneity will be assessed before pooling. Findings from the qualitative reviews will be extracted verbatim. A coding frame will be developed to undertake a content analysis of the extracted data from the included reviews.

**Analysis of subgroups or subsets**

None planned

**Dissemination plans**

The findings from this work will be disseminated through traditional academic media of conferences and peer reviewed journals but will also be circulated to relevant NHS bodies, charity partners (Asthma UK, British Lung Foundation), and other key bodies such as Quality Improvement Scotland.

**Contact details for further information**

Deborah Morrison
Academic Unit of General Practice and Primary Care, University of Glasgow,
1 Horselethill Road, Glasgow, G12 9LX, UK. Deborah.Morrison@glasgow.ac.uk

**Organisational affiliation of the review – University of Glasgow**

**Review team**

Dr Deborah Morrison, University of Glasgow
Euan Cameron, University of Glasgow
Karolina Agur, University of Glasgow
Prof Thomson, University of Glasgow
Prof Wyke, University of Glasgow
Dr Alex McConnachie, University of Glasgow
Professor Frances Mair, University of Glasgow

**Other Information:**
Details of any existing review of the same topic by the same authors - None

Anticipated or actual start date - August 2011

Anticipated completion date - July 2012

Funding sources/sponsors - Chief Scientist Office, Scotland

Conflicts of interest - None

Other registration details - None

Language - English

Country - Scotland

Key words - Asthma, self care, internet, web-based, online, computerised, quantitative, qualitative, patient education

Protocol Amendment October 2013.

Addition of search terms to.

- Keyword searches for text messaging were added;
- MeSH (Medical Subject Headings) terms “Cellular Phone” and “Social Networking” were added;
- The search terms used for mobile phones were enhanced with the addition of “smartphone$ or smart-phone$ or smart-telephone$” and associated terminology such as iPhone, app(s), Apple, Android and Blackberry;
- Newer technologies including tablet devices and social media tools were added as keyword terms;
- The terms “m-health” and “mhealth” were added to search line 29 to reflect the emergence of a new sub-field of e-health concerned specifically with mobile devices.

Electronic search updated to October 2013


Completion date – November 2013.

Protocol Amendment January 2016.

The Risk of bias (quality) assessment section is amended, to remove the following sentence:

“Those achieving 50% plus a ‘yes’ to question 7 will be included, with appropriate concessions for qualitative studies.” All studies meeting inclusion/exclusion criteria will be included and the AMSTAR score used only to describe the included reviews, and to inform discussion.

Completion date – April 2016

Reference List

Appendix 5 Meta-review search results overview and sample search strategy

The following databases and resources were searched:

- MEDLINE and MEDLINE In-Process
- EMBASE
- CINAHL
- PsycINFO
- Cochrane Database of Systematic Reviews (CDSR)
- Database of Abstracts of reviews of Effects (DARE)
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Health Technology Assessment (HTA) database
- NHS Economic Evaluation Database (NHS EED)
- ERIC (Education Resources Information Center)
- Science Citation Index (SCI)
- Social Science Citation Index (SSCI)
- DoPHER
- TRoPHI

Database results

<table>
<thead>
<tr>
<th>Resource</th>
<th>Number of results 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEDLINE and MEDLINE In-Process</td>
<td>1590</td>
</tr>
<tr>
<td>EMBASE</td>
<td>2426</td>
</tr>
<tr>
<td>CINAHL</td>
<td>1020</td>
</tr>
<tr>
<td>PsycINFO</td>
<td>155</td>
</tr>
<tr>
<td>Cochrane Database of Systematic Reviews (CDSR)</td>
<td>15</td>
</tr>
<tr>
<td>Database of Abstracts of reviews of Effects (DARE)</td>
<td>2</td>
</tr>
<tr>
<td>Cochrane Central Register of Controlled Trials (CENTRAL)</td>
<td>247</td>
</tr>
<tr>
<td>Health Technology Assessment (HTA) database</td>
<td>0</td>
</tr>
<tr>
<td>NHS Economic Evaluation Database (NHS EED)</td>
<td>4</td>
</tr>
<tr>
<td>ERIC (Education Resources Information Center)</td>
<td>16</td>
</tr>
<tr>
<td>Science Citation Index (SCI)</td>
<td>1112</td>
</tr>
<tr>
<td>Social Science Citation Index (SSCI)</td>
<td>331</td>
</tr>
<tr>
<td>DoPHER</td>
<td>12</td>
</tr>
<tr>
<td>TRoPHI</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>6952</td>
</tr>
<tr>
<td>Total once duplicates removed</td>
<td>3798</td>
</tr>
</tbody>
</table>

Sample search strategy

The search strategy used in MEDLINE (OvidSP) is shown in below (October 2013). This was adapted appropriately to run in the other databases searched.

1 (Computer or computers).hw.
2 exp computers/
3 exp Computer Systems/
4 Medical Informatics/
5 Medical Informatics Applications/
6 Decision Support Techniques/
7 Educational Technology/
8 Audiovisual Aids/
9 Telecommunications/
10 Multimedia/
Appendix 5

Metareview search strategy

11 Computer-Assisted Instruction/
12 User-Computer Interface/
13 Hypermedia/
14 Video Games/
15 Electronic Health Records/
16 Cellular Phone/
17 Social Networking/
18 (computer$ or microcomputer$ or PC or PCs or Mac or Macs or Internet or WWW or web or website$1 or webpage$ or local area network$).ti,ab.
19 software.ti,ab.
20 (cellular phone$1 or cellular telephone$1 or mobile$1 or cell phone$1 or cell telephone$1 or smartphone$ or smart-phone$ or smart-telephone$).ti,ab.
21 (handset$ or hand-set$ or wireless or wire-less or wifi or wi-fi or GPS or global positioning system$ or bluetooth or text messag$ or texting or SMS or short messag$ or multimedia messag$ or multi-media messag$ or mms or instant messag$ or social media$ or facebook or twitter or webcast$ or webinar$ or podcast$ or wiki or wikis or app or apps or Android$ or Blackberr$ or Apple$ or iOS or iphone$ or ipad$ or S40 or Symbian$ or Windows).ti,ab.
22 ((electronic$ or digital$ or device$) adj2 tablet$).ti,ab.
23 (video$ or DVD or DVDs).ti,ab.
24 (youtube or you tube or vimeo).ti,ab.
25 (online or on line or interactive).ti,ab.
26 (chat room$1 or chatroom$1).ti,ab.
27 (blog$1 or web-log$1 or weblog$1).ti,ab.
28 (bulletin board$1 or bulletinboard$1 or messageboard$1 or message board$1).ti,ab.
29 (ehealth or e-health or mhealth or m-health).ti,ab.
30 or/1-29
31 exp Asthma/
32 (asthma or asthmatic$1).ti,ab.
33 exp Anti-Asthmatic Agents/ or exp Bronchodilator Agents/
34 or/31-33
35 (action plan or action plans).ti,ab.
36 (self management or self managing).ti,ab.
37 (patient$1 adj3 manag$).ti,ab.
38 health education/
39 education.ti,ab.
40 self care/ or self administration/ or self medication/
41 self care.ti,ab.
42 self monitor$.ti,ab.
43 self treat$.ti,ab.
44 (behavior$ adj3 (chang$ or modif$ or condition$)).ti,ab.
45 Patient Satisfaction/
46 (patient$1 adj3 (experience$ or attitude$ or view$1 or satisfaction$)).ti,ab.
47 Qualitative research/
48 exp Questionnaires/
49 exp Interviews as Topic/
50 qualitative.ti,ab.
51 (interview$ or questionnaire$ or focus group$).ti,ab.
52 or/35-51
53 30 and 34 and 52
54 animals/ not humans/
55 53 not 54

Key:
/  indicates a subject heading
exp indicates an exploded subject heading
$  truncation symbol
adj3 words must appear with 3 words of each other
.ti,ab. searches are restricted to the title and abstract fields
or/1-26 combine sets 1 to 26 using OR
Appendix 6  AMSTAR 11 point checklist with guidance notes

Modified with further detail about qualitative/narrative reviews  (grey text is our own agreed rules/explanations).

1. Was an “a priori” design provided?
The research question and inclusion criteria should be established before the conduct of the review.
   It should be clearly stated that the criteria were agreed prior to the review starting, ideally with evidence of protocol registration provided. If this is not mentioned – chose can’t answer.

2. Was there duplicate study selection and data extraction?
There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.
   It should be clear that 2 people independently screened titles, abstracts and full papers AND extracted the data.
   If titles and abstracts only screened by one person then no point. If doesn’t explicitly say who screened what, then can’t answer.

3. Was a comprehensive literature search performed?
At least two electronic sources should be searched. The report must include years and databases used (e.g., Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated, and where feasible, the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.
   Answer yes if at least one other form of supplementary searching is described, with 2 databases, years searched and at least the key words provided.
   If qualitative/narrative accurate description of what has been done & why should be present and it should still be replicable from information provided.

4.a Did the authors state that they searched for reports regardless of their publication type?
The authors should state that they searched for reports regardless of their publication type. Was the status of publication (i.e., grey literature) used as an inclusion criterion? The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.

Publication type should not be used as a filter when searching for articles. However any inclusions/exclusion criteria based on publication status, language etc should be stated.

AND

4b Was the status of publication (i.e. grey literature) used as an inclusion criterion? The authors should state that they searched for
reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.

Answer no if any evidence that articles were excluded for publication type (e.g. conference proceedings, grey literature etc) or if exclusions based on language.

5. Was a list of studies (included and excluded) provided?
A list of included and excluded studies should be provided.

Included studies need to be listed in the main article. If excluded studies are not present in main body, but available as an appendix or on request from the author then can still answer yes.

6. Were the characteristics of the included studies provided?
In an aggregated form, such as a table, data from the original studies should be provided on the participants, interventions, and outcomes. The ranges of characteristics in all the studies analyzed, e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported.

Answer yes if the following criteria are present as a minimum from each original study included:
Participants – at least one participant variable described e.g. age or gender.
Intervention – intervention described beyond simple one or two word descriptions. I.e ‘internet’ or ‘patient education’ not sufficient. Outcome measured are listed.
If qualitative/narrative and no specific intervention then aim of the study should be clearly described and what ‘question’ they were trying to answer.

7. Was the scientific quality of the included studies assessed and documented?
“A priori” methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo-controlled studies, or allocation concealment as inclusion criteria); for other types of studies, alternative items will be relevant.

The method of quality assessment should be provided, with the results of the assessment provided.

8. Was the scientific quality of the included studies used appropriately in formulating conclusions?
The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.

Answer yes if the discussion and conclusion appropriately acknowledges the results of their quality assessment in coming to their conclusions.

9. Were the methods used to combine the findings of studies appropriate?
For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I2). If heterogeneity exists, a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Answer yes if the authors did not combine, and this was appropriate.

10. Was the likelihood of publication bias assessed?
If meta analysis this include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test).
If not quantitative then chose not applicable

11. Was the conflict of interest included?
Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.
Answer yes if information about conflicts of interest are made available about both the review and included studies within it. Specific detailing of sources of funding not required, unless conflict of interest present.

a ‘Can’t answer’ is chosen when the item is relevant but not described by the authors
b ‘not applicable’ is used when the item is not relevant, such as when a meta-analysis has not been possible or was not attempted by the authors.
c for clarity we split this question into two parts.
Research Partners

University of Glasgow | Institute of Health & Wellbeing

Chief Scientist Office | NHS Greater Glasgow and Clyde

With Support From

asthma UK | Chest Heart & Stroke Scotland

To find out more about the Research

Please contact:
Deborah Morrison
General Practice & Primary Care
Institute for Health and Wellbeing
1 Horselethill Road,
University of Glasgow, G62 9LY

Telephone: 0141 330 8383
Email: Deborah.Morrison@glasgow.ac.uk

Supported Self Care for Asthma
~
Development &
Evaluation of an

Focus Group & Think Aloud Studies

Study Information

If you have any concerns about the research:

Professor Graham Watt
General Practice & Primary Care
Institute for Health and Wellbeing
1 Horselethill Road,
University of Glasgow, G62 9LY

Telephone: 0141 330 9330

FGTA Participant Study Information v0.5: date 19/03/2012
Study Information Sheet

You are being invited to take part in either a focus group, a ‘think aloud’ study, or both.
Before you decide whether to take part it is important that you understand why the research is being done and what it will involve for you.
Please take some time to read the following information carefully. Feel free to discuss the study with family or friends before you decide.

Why is the study being run?
People with asthma often put up with symptoms such as wheeze, shortness of breath or interrupted sleep without realising that adjusting their inhalers might help. Some studies have shown that people with asthma have fewer symptoms when they use online resources/websites to learn about asthma and to receive feedback about their symptoms and medications. We aim to develop such a resource which will be available free of charge to people with asthma here in Scotland.
We want those who will end up using the resource, such as adults with asthma, and health professionals who look after people with asthma to be involved in the development of it. Information from the focus group will help develop a prototype of the website, which will then be tested out in ‘think aloud’ studies, described below.

Why have I been chosen?
You are being asked to take part because you have asthma. You do not need to use or own a computer to take part.

What will happen next?
If you decide you might like to take part please fill out the ‘expression of interest’ form, and post it back in the reply paid envelope. If you prefer you can phone or email the researcher Deborah Morrison (details overleaf). We will contact you to discuss the two types of studies, & any practical arrangements such as your availability.

What will taking part in the focus group mean for me?
The focus groups will be a mix of adults with asthma, like yourself, and practice nurses who undertaken asthma reviews. The focus groups will take place at the Department of General Practice and Primary Care, University of Glasgow (see overleaf for details). You will be asked about your experience of managing your asthma, and what sort of role the internet could have in helping you do this. The discussion will be audio recorded and will take approximately 90 minutes, but we would ask you to be available for up to 3 hours.

What will taking part in a ‘think aloud’ study mean for me?
In order to make sure that this online resource/ website is easy to use and well designed we need people to test it during its development phase. This involves using the website, and as you go through the pages we ask you to say out loud what you are thinking – what you like and what you don’t like. This is audio recorded, and the researcher will also be taking notes. At the end you will have the opportunity to feedback any general comments about the website. Think aloud studies can take place at either the Department of General Practice and Primary Care at Glasgow University (see overleaf for details), or your own home, whichever you prefer, and will take ~ 2 hours.

What information do you require?
Before either type of study we will go over the consent form and ensure it is signed, and ask you to fill out some basic information about yourself (age, gender, years since diagnosis, asthma medications, hospitalisations and a short questionnaire about your symptoms).

Who is running the study?
The study is being conducted at the University of Glasgow. It is funded by the Chief Scientist Office (CSO) Scotland, and is sponsored by NHS Greater Glasgow & Clyde.

Do I have to take part?
No. It is up to you to decide whether to take part or not. You can choose to take part in either the focus group, think aloud study or if you wish both.

Will I benefit from taking part?
The information gathered here should help to improve the future care of people with asthma. There may be no direct benefit to you for taking part, although some people find it helpful talking about their asthma. Please note no changes to treatments can be made by the research team.

Are there any risks involved?
There are no identifiable risks to you taking part in this study.

Can I change my mind?
Yes. You can withdraw from the study at any time without giving a reason.

Can people find out that I have taken part?
No. All information which is collected about you during this study will be kept strictly confidential. Any information about you will have your identifiable details removed so you cannot be recognised.

What will happen to the results?
The information we gather will help us to design the website. We plan to publish the results in relevant medical journals, so that other researchers can learn from the study. All information used will be anonymised so any report or journal articles published will not identify you or any other individual taking part.
The website will then be tested in a trial setting to see how it is used in day to day life by people with asthma.

Expenses
You will be given a £20 gift voucher for taking part to compensate for your time. In addition a form will be provided to allow you to claim travel expenses.
Research Partners

University of Glasgow | Institute of Health & Wellbeing

CHIEF SCIENTIST OFFICE

NHS Greater Glasgow and Clyde

Supported Self Care for Asthma
~ Development &
Evaluation of an Online Resource

Focus Group Studies:
Adults with Asthma & Practice Nurses.

Study Information Sheet

To find out more about the Focus Group Research

Please contact:
Deborah Morrison
General Practice & Primary Care
Institute for Health and Wellbeing
1 Horselethill Road,
University of Glasgow, G12 9LX

Telephone: 0141 330 8383
Email: Deborah.Morrison@glasgow.ac.uk

If you have any concerns about the research:

Professor Graham Watt
General Practice & Primary Care
Institute for Health and Wellbeing
1 Horselethill Road,
University of Glasgow, G12 9LX

Telephone: 0141 330 8330
Study Information Sheet

You are being invited to take part in a focus group study to help us understand how we can help people with asthma manage their condition more effectively.

Before you decide whether to take part in the study, it is important that you understand why the research is being done and what it will involve for you.

Please take time to read the following information carefully.

Why is the study being run?

You will know from undertaking asthma reviews that people with asthma often put up with symptoms such as wheezing, shortness of breath or interrupted sleep without realising that adjusting their inhalers might help. Some studies have shown that people with asthma have fewer symptoms and lifestyle limitations when they use online resources to learn about asthma and to receive feedback about their symptoms and medications. We are aiming to develop such a resource which will be available free of charge to people with asthma here in Scotland.

We want those who will end up using the resource, such as adults with asthma, and health professionals who look after people with asthma to be involved in the development of it. We hope it will be a resource you feel able to direct your patients to.

Why have I been chosen?

You are being asked to take part because in your role as a practice nurse undertaking asthma reviews you have an understanding of the difficulties which people face when trying to manage their asthma, and are therefore well placed to try and help us understand what features of an online tool would make it easier.

What will happen next?

If you decide you might like to take part please fill out the ‘expression of interest’ form which you received along with this information leaflet. This can be posted back in the reply paid envelope, or if you prefer you can phone or email the researcher Deborah Morrison (details overleaf).

Once this has been received we will contact you to discuss the study itself, and any practical arrangements such as availability for the groups to take place.

What will taking part in the study mean for me?

We intend to have a mix of adults with asthma (4-6) and practice nurses (2-3) in the group. The focus groups will take place at the Department of General Practice and Primary Care at Glasgow (see overleaf for details).

When you arrive we will go over the consent form which you received with this leaflet to ensure it is signed, and ask you to fill out some basic information about yourself (normal place of work, years trained, and years experience of undertaking asthma reviews).

We will then start the discussion. This will be audio recorded, so that a transcription of the discussion can be typed, at which point all identifying details will be removed.

We want to try and establish what features of an online resource would be attractive to potential users and what barriers there would be to it being used.

Overall, including time at the start for filling out the forms we expect this to take approximately 2-3 hours of your time.

Who is running the study?

The study is being conducted at the University of Glasgow. It is funded by the Chief Scientist Office (CSO) Scotland, and is sponsored by NHS Greater Glasgow & Clyde.

Do I have to take part?

No. It is up to you to decide whether to take part or not.

Will I benefit from taking part?

The information gathered here should help to improve the future care of people with asthma. There may be no direct benefit to you for taking part, although you might find some useful insights about asthma self management that may help in your day to day clinical work.

Are there any risks involved?

There are no identifiable risks to you taking part in this study.

Can I change my mind?

Yes. You can withdraw from the study at any time without giving a reason.

Can people find out that I have taken part?

No. All information which is collected about you during this study will be kept strictly confidential. Any information about you will have your identifiable details removed so you cannot be recognised.

What will happen to the results?

The information we gather will help us to design the website. This will be then be tested by adults with asthma during its development phase, and evaluated in a pilot trial. We plan to publish the results in relevant medical journals, so that other researchers can learn from the study. All information used will be anonymised so any report or journal articles published will not identify you or any other individual taking part.

Expenses

You (or your practice if you attend the focus group in work time) will be reimbursed £23/hr. In addition a form will be provided to allow you to claim travel expenses.
Appendix 9 Focus group topic guide

The contents of this focus group guide will be informed by the finding of the ongoing literature review so may be subject to some changes in content.

**Background:** I will give a short (10 minute) presentation about asthma, the finding of the systematic review of all qualitative and quantitative reviews of online interactive self care asthma resources, and a review of the qualitative literature about knowledge and understanding of asthma.

**The following issues will then be addressed/explored:**

**Topic 1: Respond to the information presented, gain current understanding of potential role of online resource. (coherence)**

What do you the participants think about the information reported in the current literature?

**Probe:** What do they agree with? What do they disagree with? Specifically focusing on the notion of online self help – what are perceptions/ideas about the role of an online intervention?

**Topic 2: Are potential users of the resource open to the idea of an online self management website? (cognitive participation)**

Who or what helps participants just now to help manage their asthma? What do they think are the barriers and facilitators to use of an asthma tool?

**Probe:** Who do they engage with – family, friends, or health professionals? What role do they take themselves? What are participants’ views about using an online tool? What are participants’ views about others having access to their information on the online tool – e.g. family, health professionals? GP practices could receive email updates automatically from the resource about changes in medication? What about automatic email or text reminders to use the resource? What would help to sustain use? What do practice nurses feel about such a resource, would they anticipate using it in consultation?

**Topic 3: What do people do currently to manage their asthma, and what role might an online resource have? (collective action)**

What tools are used currently – why – what are the benefits, drawbacks?

**Probe:** What makes managing asthma difficult? Can barriers to use of internet resources be identified? Would it be compatible with current ways asthma is managed? Would there be concerns about the technology or confidentiality? What would make it attractive? What would put them off?

To prompt this I could show examples of currently available online asthma resources e.g. you tube video of inhaler technique, asthma UK information, NHS websites. What features of an online resource would people with asthma, and practice nurses like to see incorporated into the development of this one.
**Topic 4: What features would participants like to see, to provide evidence that the intervention is helpful (reflexive monitoring)**

What would be a sign to them that the intervention is having the desired effect?

**Probe:** How would they decide it is working? What outcomes would they like to see to show it was worth continuing to keep using it? What would put them off? How would participants feel about being involved in trying out the intervention during the development phase, in order to feedback and improve it?

**Any further areas of discussion:**

- Do any of the participants have anything further to add from what we have discussed today?

**Give thanks for participating.**
Aim of intervention: reduce burden of symptoms and increase QOL through supporting use of medications.

Methods: Statements relating to adherence specifically were extracted from a previously undertaken literature review. A relevant feature of the proposed website was attributed to the statement, resulting in a ‘suggested component’ to be a feature of the website. This led to the production of tables showing barriers and enablers from the literature. Two articles were of specific relevance and these were looked at in detail individually, and tables relevant to their findings also produced in the same way as described above (GINA guidelines[1], chapter 4, and a review of adherence[2]. Finally analysis of the two focus groups provided information for a further set of tables describing identified barriers and enablers. Finally the information relevant to each component was grouped together to produce a table for each, illustrating the source of the evidence.
### Component: Info page – on medication & side-effects with suggestions of alternatives to avoid these side-effects

<table>
<thead>
<tr>
<th>Source</th>
<th>Finding relevant to adherence</th>
<th>Suggested feature of website.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma literature review</td>
<td>People with asthma's beliefs about medications can impact on adherence.[1, 3](E.g., effectiveness, tolerance, fears of side-effects)</td>
<td>Provide information to challenge beliefs both facts and experiences.</td>
</tr>
<tr>
<td>GINA guidelines chapter 4, component 1 – key components of successful asthma education programme.[1]</td>
<td>• Potential side-effects</td>
<td>Information describing side effects and possible alternative treatments to minimise them.</td>
</tr>
<tr>
<td>• Use of inhaler device</td>
<td></td>
<td>Info to illustrate different inhalers, and inhaler technique, combined with videos demonstrating technique.</td>
</tr>
<tr>
<td>• Difference between relievers and preventers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adherence review[2]: DiMatteo MR et al. <em>Health Psychology Review 2012; 6(1):74-91.</em></td>
<td>An individual's beliefs about the value of the treatment (i.e. likely risks, benefits and efficacy) and their confidence that practical barriers to adherence can be overcome are also meaningful in influencing motivation to adhere.</td>
<td>Information section about medications – risks, benefits. Quotes illustrating positive experience of patients who started taking medication and then felt better for example</td>
</tr>
<tr>
<td>Focus group</td>
<td>Problems with medications (side-effects/inhaler technique) as a barrier to adherence could be overcome by acknowledging potential issues with advice about alternatives.</td>
<td>Information section about medications Provide examples of identified barriers to adherence from literature to help user identify any relevant to self with potential strategies to overcome.</td>
</tr>
</tbody>
</table>

### Component: Info page – benefits of an AAP

<table>
<thead>
<tr>
<th>Source</th>
<th>Finding relevant to adherence</th>
<th>Suggested feature of website.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma literature review</td>
<td>People with asthma with a new diagnosis lacked confidence in using action plans.[4]</td>
<td>Illustrate benefits &amp; low risk of harms.</td>
</tr>
<tr>
<td>People with asthma feel that action plans are not relevant to their situation.[5] *Those described as compliant (taking optimal doses of both reliever and preventer) felt action plans do not acknowledge their own experience, irrelevant * Those described as non-compliant felt that action plans could be useful for people with “more serious” or “proper” asthma.</td>
<td>Provide info to illustrate benefits of asthma action plan.</td>
<td></td>
</tr>
</tbody>
</table>
### Component: Info page – how to use an AAP, including quotes/videos where applicable, incorporating the role of goals.

<table>
<thead>
<tr>
<th>Source</th>
<th>Finding relevant to adherence</th>
<th>Suggested feature of website.</th>
</tr>
</thead>
</table>
| Asthma literature review | People with asthma with a new diagnosis lacked confidence in using action plans.[4] | Provide information about how to use action plans  
Provide examples of using AAP use, quotes aiming to increase confidence |
| Guided self-management with asthma plan (including health professional review improves asthma related outcomes).[6] | Information pages about how to self-manage e.g. self-monitor, use an AAP, role of goals in self-management |
| Self-management education improves action plan use.[7] | Info page about how to use an action plan  
Provide examples of using AAP, quotes aiming to increase confidence in use |
| Focus group | Provide information about how to self-manage to facilitate adherence. | Info pages – how to use AAPs and benefits of using them. |


<table>
<thead>
<tr>
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<th>Finding relevant to adherence</th>
<th>Suggested feature of website.</th>
</tr>
</thead>
</table>
| Asthma literature review | People with asthma are poor at recognising deterioration in asthma symptoms, and therefore unable to act appropriately.[4] | Provide info how to self-monitor  
Provide info to show benefits of self-monitoring |
| Guided self-management with asthma plan (including health professional review improves asthma related outcomes).[6] | Information pages about how to self-manage e.g. self-monitor, use an AAP, role of goals in self-management. Provide action plans |
| Self-monitoring in order to recognise loss of asthma control is a grade A recommendation within the BTS/SIGN guidelines.[8]. | Info about how to monitor self for deterioration in symptoms |
| Weekly monitoring may be sufficient in those with well or partly controlled asthma, and that this could safely become less frequent once good control is achieved.[9] | Info about how to monitor self for deterioration i.e. symptoms or via PEF monitoring, and how often to monitor. |
| GINA guidelines chapter 4, component 1 – key components of successful asthma education programme.[1] | • Signs that suggest asthma is worsening and actions to take.  
• Monitoring control of asthma. | Info about how to monitor self for deterioration in symptoms. |
<p>| Adherence review[2]: DiMatteo MR et al. Health Psychology Review 2012; 6(1):74-91. | Multifaceted approaches work best involving combinations of strategies such as providing information and reminders, simplifying behaviour required, practicing ongoing assessment, counselling, self-monitoring and providing reinforcements. | Intervention will utilise combination of strategies: information provision, tools for self-monitoring, reminder emails |
| Focus group | Provide information about how to self-manage to facilitate adherence. | Info pages – how to self-monitor recognising deteriorating symptoms |</p>
<table>
<thead>
<tr>
<th>Component: Info page - challenge attitude (denial) and illustrate benefits of accepting diagnosis, and taking medications. Using quotes where applicable.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Source</strong></td>
</tr>
<tr>
<td>Asthma literature review</td>
</tr>
<tr>
<td>GINA guidelines chapter 4, component 1 – key components of successful asthma education programme.([1])</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Adherence review[2]: DiMatteo MR et al. <em>Health Psychology Review</em> 2012; 6(1):74-91.</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Focus group</td>
</tr>
</tbody>
</table>
### Component: Info – common barriers to adherence and suggestions to overcome

<table>
<thead>
<tr>
<th>Source</th>
<th>Finding relevant to adherence</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Asthma literature review</td>
<td>Having the same type of inhaler for reliever and preventer improves outcomes of asthma control and exacerbation rate.[13]</td>
<td>Help patients to identify barriers to taking meds and if complicated regime contributing then encourage discussion with health professional.</td>
</tr>
<tr>
<td>Adherence review[2]: DiMatteo MR et al. <em>Health Psychology Review</em> 2012; 6(1):74-91.</td>
<td>People with asthma must have the tools and strategies necessary and must have the capacity to overcome barriers to adherence – so important task for health professional is help patient identify and overcome barriers to adherence.</td>
<td>Provide examples of identified barriers from literature to help user identify any relevant to self. E.g. if recognise a complicated regime contributing then encourage discussion with health professional.</td>
</tr>
<tr>
<td></td>
<td>A complex treatment regime is one of the most consistent barriers to successful adherence.</td>
<td>Help patients to identify barriers to taking meds. If complicated regime contributing then encourage discussion with health professional.</td>
</tr>
<tr>
<td></td>
<td>People with asthma must have the tools and strategies necessary and must have the capacity to overcome barriers to adherence – so important task for health professional is help patient identify and overcome barriers to adherence.</td>
<td>Provide examples of identified barriers from literature to help user identify any relevant to self. E.g. if recognise a complicated regime contributing then encourage discussion with health professional.</td>
</tr>
<tr>
<td></td>
<td>An individual’s beliefs about the value of the treatment (i.e. likely risks, benefits and efficacy) and their confidence that practical barriers to adherence can be overcome are also meaningful in influencing motivation to adhere.</td>
<td>Provide examples of identified barriers from literature to help user identify any relevant to self. List provided in figure 4.1-4 GINA guidelines[1] page and potential strategies to overcome. E.g. if recognise a complicated regime contributing then encourage discussion with health professional.</td>
</tr>
<tr>
<td>Focus group</td>
<td>Problems with medications (side-effects/inhaler technique) as a barrier to adherence could be overcome by acknowledging potential issues with advice about alternatives.</td>
<td>Provide examples of identified barriers to adherence from literature to help user identify any relevant to self, and potential strategies to overcome.</td>
</tr>
</tbody>
</table>

### Component: Provide links to relevant websites

<table>
<thead>
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</thead>
<tbody>
<tr>
<td>Adherence review[2]: DiMatteo MR et al. <em>Health Psychology Review</em> 2012; 6(1):74-91.</td>
<td>Mental health issues represent another common barrier to successful adherence, and health professionals should assess for the presence of such issues</td>
<td>Point out this can be a barrier and provide links to relevant websites e.g. <a href="http://www.glasgowsteps.com">www.glasgowsteps.com</a> or advice to discuss with health professional.</td>
</tr>
</tbody>
</table>
### Component: Info page – benefits of, and getting the most out of, the annual review

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<thead>
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</thead>
<tbody>
<tr>
<td>Asthma literature review</td>
<td>Goal setting has been a component of successful interventions in asthma, with patient centred goals described.[14]</td>
<td>Encourage user to consider goals to discuss at annual review.</td>
</tr>
<tr>
<td></td>
<td>Guided self-management with asthma plan (including health professional review improves asthma related outcomes.[6]</td>
<td>Information pages about role of annual review.</td>
</tr>
<tr>
<td></td>
<td>Shared decision making (incorporating patient goals and preferences into the consultation) improved adherence to medication and clinical outcomes.[15]</td>
<td>Encourage user to consider goals to discuss at annual review.</td>
</tr>
</tbody>
</table>
| GINA guidelines chapter 4, component 1 – key components of successful asthma education programme.[1] | • Development of a partnership between patient and health professional.  
• Sharing of information. | Provide info about benefits of attending for health professional review. |
| Adherence review[2]: DiMatteo MR et al. Health Psychology Review 2012; 6(1):74-91. | A complex treatment regime is one of the most consistent barriers to successful adherence. | Help patients to identify barriers to taking meds. If complicated regime contributing then encourage discussion with health professional. |
| | Mental health issues represent another common barrier to successful adherence, and health professionals should assess for the presence of such issues. | Point out this can be a barrier and provide links to relevant websites e.g www.glasgowsteps.com with advice to discuss with health professional. |
| | When individuals are adequately informed, they are better able to share in the decisions that affect their health, and are more committed to regimes that they have had a part in choosing. | Set up reminder email prior to date of due annual review, suggesting user visits website prior to annual review. Info about what to expect from the annual review and how to get the most from it. |
| Focus group | Participants keen to have face to face contact as part of the asthma review. | Information about getting the most of the annual review. |

### Component: Facilitating recall - self test quizzes

<table>
<thead>
<tr>
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<th>Suggested feature of website, specific to component.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adherence review[2]: DiMatteo MR et al. Health Psychology Review 2012; 6(1):74-91.</td>
<td>Providing information to individuals is essential, but not sufficient to ensure adherence. More information leads to improved recall (but patients can become overwhelmed) and better outcomes when physicians assess patients’ recall.</td>
<td>Provide optional self test quizzes</td>
</tr>
<tr>
<td></td>
<td>When individuals understand clearly and remember what they are asked to do, they are much more likely to do it.</td>
<td>Self test quizzes may aid recall, as will option to print specific pages</td>
</tr>
<tr>
<td>Component: Info provided must be consistent with that provided by health care professionals and relevant charities.</td>
<td>Source</td>
<td>Finding relevant to adherence</td>
</tr>
<tr>
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</tr>
<tr>
<td>Adherence review[2]: DiMatteo MR et al. Health Psychology Review 2012; 6(1):74-91.</td>
<td>There is evidence that during the medical visit physicians consistently omit critical elements of information regarding medication use, thus contributing to non-adherence.</td>
<td>Content of website to be consistent with guideline recommendations, so will mirror what is discussed with health professionals.</td>
</tr>
<tr>
<td>Focus group</td>
<td>Length of time between annual reviews – difficult to retain the information.</td>
<td>Provide info which mirrors that discussed during annual review, and can be revisited by user at any time.</td>
</tr>
<tr>
<td></td>
<td>Website to bridge the gap between asthma reviews by being source of information, and reminders (e.g. hay fever season, flu jab due).</td>
<td>Information will be available at all times via website, and will mirror that discussed in annual asthma reviews.</td>
</tr>
<tr>
<td></td>
<td>Website being recommended by nurses during asthma reviews.</td>
<td>Information will mirror that discussed in annual asthma reviews.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Component: Tailored asthma action plan</th>
<th>Source</th>
<th>Finding relevant to adherence</th>
<th>Suggested feature of website, specific to component.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma literature review</td>
<td>People with asthma find action plans are not relevant or useful to their own situation[11]</td>
<td>Tailor asthma action plans (e.g. to severity, experience, goals) in the context of living with asthma plan.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>People with asthma feel that action plans are not relevant to their situation.[5] *Those described as compliant (taking optimal doses of both reliever and preventer) felt action plans do not acknowledge their own experience, irrelevant * Those described as non-compliant felt that action plans could be useful for people with “more serious” or “proper” asthma.</td>
<td>Tailor action plan based on severity.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Several meta-analysis have highlighted the importance of tailoring to obtain optimum effectiveness</td>
<td>Action plans can be tailored where possible.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Component: Diary tool for keeping track of medication used</th>
<th>Source</th>
<th>Finding relevant to adherence</th>
<th>Suggested feature of website, specific to component.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focus group</td>
<td>Difficult to keep track of what medication has been used, and need for ordering more. Would like means to track medication use, particularly reliever medication.</td>
<td>Provide a diary tool for keeping track of medication use.</td>
<td></td>
</tr>
</tbody>
</table>
## Component: Tool for monitoring e.g. ACT or ACQ or PEF diary/calculator

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</thead>
<tbody>
<tr>
<td>Asthma literature review</td>
<td>People with asthma overestimate their control and tolerate unnecessary symptoms[16]:</td>
<td>Provide tool to assess control/symptoms e.g. ACT, ACQ</td>
</tr>
<tr>
<td></td>
<td>People with asthma are poor at recognising deterioration in asthma symptoms, and therefore unable to act appropriately[4]:</td>
<td>Provide tools for self-monitoring e.g. ACT, ACQ with resultant action plans to ensure appropriate action taken.</td>
</tr>
<tr>
<td></td>
<td>People with asthma alter medications inappropriately in response to a perceived deterioration in symptoms.[17]:</td>
<td>Tool to aid assessment of current control either by PEF or symptom score</td>
</tr>
<tr>
<td></td>
<td>Self-monitoring in order to recognise loss of asthma control is a grade A recommendation within the BTS/SIGN guidelines.[8]:</td>
<td>Info about how to monitor self for deterioration in symptoms</td>
</tr>
<tr>
<td></td>
<td>Weekly monitoring may be sufficient in those with well or partly controlled asthma, and that this could safely become less frequent once good control is achieved,[9]:</td>
<td>Tool to use to assess current control either symptom score or PEF</td>
</tr>
<tr>
<td></td>
<td>GINA guidelines chapter 4, component 1 [1]:</td>
<td>Provision of tools to facilitate self-monitoring.</td>
</tr>
<tr>
<td></td>
<td>• Signs that suggest asthma is worsening, and actions to take</td>
<td>Tool to establish current level of control, and advice on action to take.</td>
</tr>
<tr>
<td></td>
<td>• Monitoring control How and when to seek medical attention</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Prevention of symptoms and attacks</td>
<td></td>
</tr>
<tr>
<td>Adherence review[2]: DiMatteo MR et al. Health Psychology Review 2012; 6(1):74-91.</td>
<td>Multifaceted approaches work best involving combinations of strategies such as providing information and reminders, simplifying behaviour required, practicing ongoing assessment, counselling, self-monitoring and providing reinforcements.</td>
<td>Intervention will utilise combination of strategies: information provision, tools for self-monitoring, reminder emails</td>
</tr>
<tr>
<td></td>
<td>Not being prepared for flare – either unexpected worsening of symptoms, or for time of year when symptoms regularly more problematic.</td>
<td>Provide tool to establish if control is poor e.g. ACT, ACQ</td>
</tr>
<tr>
<td></td>
<td>Provide information about how to self-manage to facilitate adherence.</td>
<td>Use of reminder emails e.g. in spring in case worsens with pollen.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Info pages – how to self-monitor recognising deteriorating symptoms, how to use AAPs and benefits of using them. How to recognise barriers to adherence. Tools – to monitor self either with symptoms (ACQ or ACT) or via PEF (via calculator or diary). Tools to promote adherence e.g. using goal setting AAP.</td>
</tr>
</tbody>
</table>

## Component: Diary tool for keeping track of medication used

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<tbody>
<tr>
<td>Focus group</td>
<td>Difficult to keep track of what medication has been used, and need for ordering more. Would like tracker, particularly reliever medication.</td>
<td>Provide a diary tool for keeping track of medication use.</td>
</tr>
</tbody>
</table>
### Component: Email reminders

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Asthma literature review</td>
<td>Guided self-management with asthma plan (including health professional review improves asthma related outcomes.[6])</td>
<td>Email reminders about attending for health professional review</td>
</tr>
<tr>
<td></td>
<td>Shared decision making (incorporating patient goals and preferences into the consultation) improved adherence to medication and clinical outcomes.[15]</td>
<td>Email reminders to encourage viewing of website prior to annual review</td>
</tr>
</tbody>
</table>
| GINA guidelines chapter 4, component 1 – key components of successful asthma education programme.\[1\] | • Development of a partnership between patient and health professional.  
• Sharing of information. | Email reminders to facilitate attendance at review |
|        | • Person then requires regular supervision, revision, reward, reinforcement | Occasional email reminders to think about recent control e.g RCP 3 questions, if haven’t logged on for a set time period. ‘Congratulations’ message if consistently demonstrates good control when using assessment tool. If achieve preset goal, then receive email or message recognising this. |
| Adherence review[2]: DiMatteo MR et al. *Health Psychology Review* 2012; 6(1):74-91. | Multifaceted approaches work best involving combinations of strategies such as providing information and reminders, simplifying behaviour required, practicing ongoing assessment, counselling, self-monitoring and providing reinforcements. | Intervention will utilise combination of strategies: information provision, tools for self-monitoring, reminder emails |
|        | It is crucial to assess, and to regularly track the continuing adherence status of individual patients as it is one of the best ways to estimate future behaviour. | Occasional email reminders to think about recent control e.g RCP 3 questions, if haven’t logged on for a set time period. |
|        | When individuals are adequately informed, they are better able to share in the decisions that affect their health, and are more committed to regimes that they have had a part in choosing. | Set up reminder email prior to date of due annual review, suggesting user visits website prior to annual review. |
| Focus group | Not being prepared for flare – either unexpected worsening of symptoms, or for time of year when symptoms regularly more problematic. | Use of reminder emails e.g. in spring in case worsens with pollen. |
|        | Website to bridge the gap between asthma reviews by being source of information, and reminders (e.g. hay fever season, flu jab due). | Email reminders |
|        | Providing means to track use of medications, or flag up need to order meds in. | Email reminders |
## Component: Make visually appealing and accessible as possible e.g. graded Info, videos, images, option to print pages relevant to the individual

<table>
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<th>Source</th>
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</thead>
<tbody>
<tr>
<td>Asthma literature review</td>
<td>Impaired literacy is associated with reduced asthma knowledge and improper inhaler use,[18] reduced aural literacy is associated with poorer asthma control measured by nights with symptoms.[19]</td>
<td>Provide information in a graded way, where user can determine depth of information required. Use images, videos.</td>
</tr>
<tr>
<td>GINA guidelines chapter 4, component 1.[1]</td>
<td>• Use of inhaler devices • Difference between relievers and preventers</td>
<td>Info to illustrate different inhalers, and inhaler technique, combined with videos demonstrating technique</td>
</tr>
<tr>
<td>Adherence review[2]: DiMatteo MR et al. Health Psychology Review 2012; 6(1):74-91.</td>
<td>Individuals are only capable of doing what they clearly understand; unintentional non-adherence is often rooted in failures at this stage of the process.</td>
<td>User can determine depth of information by presenting info in graded form. Provide information which has undergone user review (think aloud studies) to optimise users ability to understand it.</td>
</tr>
<tr>
<td></td>
<td>There is evidence that during the medical visit physicians consistently omit critical elements of information regarding medication use, thus contributing to non-adherence.</td>
<td>Providing alternative comprehensive source of information available 24/7 via a website.</td>
</tr>
<tr>
<td></td>
<td>Several meta-analysis have highlighted the importance of tailoring to obtain optimum effectiveness</td>
<td>User can determine depth of information by presenting info in graded form.</td>
</tr>
<tr>
<td></td>
<td>Providing information to individuals is essential, but not sufficient to ensure adherence. More information leads to improved recall (but patients can become overwhelmed) and better outcomes when physicians assess patients’ recall.</td>
<td>Provide a ‘print this page’ button so that users can print off particular pages that are relevant to them.</td>
</tr>
<tr>
<td></td>
<td>When individuals understand clearly and remember what they are asked to do, they are much more likely to do it.</td>
<td>User can determine depth of information by presenting info in graded form. Provide information which has undergone user review (think aloud studies) to optimise users ability to understand it.</td>
</tr>
<tr>
<td>Focus group</td>
<td>Length of time between annual reviews – difficult to retain the information.</td>
<td>Provide info which mirrors that discussed during annual review, and can be revisited by user at any time. ‘Print this page option’</td>
</tr>
<tr>
<td></td>
<td>Staggering the available information to be relevant as possible</td>
<td>User can determine depth of information by presenting info in graded form. Provide information which has undergone user review (think aloud studies) to optimise users ability to understand it.</td>
</tr>
<tr>
<td></td>
<td>Website to bridge gap between asthma reviews: source of information, reminders (e.g. hay fever season, flu jab due).</td>
<td>Information will be available at all times via website, and will mirror that discussed in annual asthma reviews</td>
</tr>
<tr>
<td></td>
<td>Making the information fun and attractive.</td>
<td>Provide information which has undergone user review (think aloud studies) to optimise users ability to understand it. Use images and videos where relevant.</td>
</tr>
</tbody>
</table>
### Component: Asthma action plan (AAP)

<table>
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<tr>
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</tr>
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<tbody>
<tr>
<td>Asthma literature review</td>
<td>Health professionals don’t always offer action plans[4, 5, 20]</td>
<td>Provide alternative means of accessing action plan via freely available website</td>
</tr>
<tr>
<td></td>
<td>People with asthma are poor at recognising deterioration in asthma symptoms, and therefore unable to act appropriately.[4]</td>
<td>Provide tools for self-monitoring e.g. ACT, ACQ with resultant action plans to ensure appropriate action taken.</td>
</tr>
<tr>
<td></td>
<td>People with asthma alter medications inappropriately in response to a perceived deterioration in symptoms.[17]</td>
<td>Provide action plan to guide medication alteration</td>
</tr>
<tr>
<td></td>
<td>Health professionals belief that actions plans only suitable for certain patients – e.g. well educated with well controlled asthma. [5]</td>
<td>Provide alternative means of accessing action plan via freely available website</td>
</tr>
<tr>
<td>GINA guidelines chapter 4, component 1 – key components of successful asthma education programme.[1]</td>
<td>Guided self-management with asthma plan (including health professional review improves asthma related outcomes.[6]</td>
<td>Provide action plans</td>
</tr>
</tbody>
</table>
|                                       | • Monitoring control of asthma  
• How and when to seek medical attention  
• Prevention of symptoms and attacks  
• Person then requires a written asthma action plan                                                                                                           | Provision of AAP to guide medication changes, changes to monitoring frequency, or to suggest health professional review. |
|                                       |                                                                                                                                                                                                                               | Tool to establish current level of control, and advice on action to take. |
| Focus group                           | Provide information about how to self-manage to facilitate adherence.                                                                                                                                                       | Tools to promote adherence e.g. using goal setting and AAP. |

### Component: Info - encourage positive involvement of family/friends in management

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Asthma literature review</td>
<td>Role of social relationships can negatively impact on people with asthma ability to self-manage, e.g. perceived ‘nagging’ from family members to take medication, over reactions, or indifference.[21]</td>
<td>Provide page aimed at family/friends about how can support the person with asthma to manage their asthma as well as possible</td>
</tr>
<tr>
<td></td>
<td>Positive social relationships e.g. helpful reminders to take medications.[21]</td>
<td>Provide info to illustrate potential beneficial role of family friends, with page targeted to family or friends.</td>
</tr>
<tr>
<td>Adherence review[2]: DiMatteo MR et al. Health Psychology Review 2012; 6(1):74-91.</td>
<td>Cultural norms, family members and friends also strongly influence patients’ decisions about health actions – particularly through their goals and intentions – and adherence to treatment is no exception.</td>
<td>Provide info page targeted at family/friends to encourage positive influence on adherence.</td>
</tr>
</tbody>
</table>
### Component: Menu of template goals with associated action plans to achieve goal

<table>
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</thead>
<tbody>
<tr>
<td><strong>Asthma literature review</strong></td>
<td>Goal setting has been a component of successful interventions in asthma, and patient centred goals described.[14] More holistic approach to actions plans – ‘living with asthma plan’. [10, 11]</td>
<td>Provide menu template goals (lifestyle rather than medication) Provide action plans to facilitate goal achievement (not just medication related, could be exercise, self-monitoring, stopping smoking) Relates to tone of the intervention — template goals provided with relevant advice to achieve goal relevant to individual. Provide template goals (lifestyle rather than medication) with associated action plans to help achieve goals. Explain can aim for minimum symptoms, and minimum impact of day to day life, provide sample ‘goals’ for patients to select which are relevant to own life, based on this qualitative work.</td>
</tr>
<tr>
<td><strong>GINA guidelines chapter 4, component 1 – key components of successful asthma education programme.</strong>[1]</td>
<td>• Discussion of expectations</td>
<td>Explain can aim for minimum symptoms, and minimal impact on day to day life, provide sample ‘goals’ for patients to select. Provide AAPs to facilitate goal achievement.</td>
</tr>
<tr>
<td><strong>Focus group</strong></td>
<td>Provide information about how to self-manage to facilitate adherence.</td>
<td>Tools to promote adherence e.g. using goal setting and AAP.</td>
</tr>
</tbody>
</table>

### Component: Tailored asthma action plan

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td><strong>Asthma literature review</strong></td>
<td>People with asthma find action plans are not relevant or useful to their own situation[11] People with asthma feel that action plans are not relevant to their situation.[5] <em>Those described as compliant (taking optimal doses of both reliever and preventer) felt action plans do not acknowledge their own experience, irrelevant</em> *Those described as non compliant felt that action plans could be useful for people with “more serious” or “proper” asthma. Several meta-analysis have highlighted the importance of tailoring to obtain optimum effectiveness</td>
<td>Tailor asthma action plans (e.g. to severity, experience, goals) in the context of living with asthma plan Tailor action plan based on severity Action plans can be tailored where possible.</td>
</tr>
</tbody>
</table>

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1. [14]
2. [10, 11]
3. [15]
4. [22]
AAP – Asthma action plan (this can refer to a plan advising about altering medications, monitoring regimes, when to seek health professional review); ACQ – Asthma control questionnaire; ACT – Asthma Control Test; PEF – peak expiratory flow; RCP 3Q – Royal College Physicians 3 Questions (to assess control)

References (Intervention Planning document, appendix 12)

Dear Dr Morrison

Study Title: A Pilot Randomised Controlled Trial of Asthma Internet Self Management Intervention. The RAISIN Study.

REC reference: 13/WS/0004
Protocol number: GN12RM562
IRAS project ID: 120011

The Research Ethics Committee reviewed the above application at the meeting held on 11 January 2013. Thank you for attending to discuss the application.

Documents reviewed

The documents reviewed at the meeting were:

<table>
<thead>
<tr>
<th>Document</th>
<th>Version</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covering Letter</td>
<td>-</td>
<td>17 December 2012</td>
</tr>
<tr>
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<td>-</td>
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</tr>
<tr>
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<td>1.1</td>
<td>13 December 2012</td>
</tr>
<tr>
<td>Investigator CV</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Letter of invitation to participant</td>
<td>1.0</td>
<td>13 December 2012</td>
</tr>
<tr>
<td>Participant Information Sheet: Leaflet</td>
<td>1.0</td>
<td>13 December 2012</td>
</tr>
<tr>
<td>Participant Consent Form</td>
<td>1.0</td>
<td>13 December 2012</td>
</tr>
<tr>
<td>GP/Consultant Information Sheets</td>
<td>1.0</td>
<td>13 December 2012</td>
</tr>
<tr>
<td>Advertisement</td>
<td>1.0</td>
<td>13 December 2012</td>
</tr>
<tr>
<td>Evidence of insurance or indemnity</td>
<td>-</td>
<td>08 August 2012</td>
</tr>
</tbody>
</table>
Provisional opinion

Ethical issues raised by the Committee in private discussion, together with responses given by the researcher when invited into the meeting:

1. The Committee asked the researchers for information regarding the online self management resource. You explained that it is a standalone website which is still under construction, which can be accessed as often as required, with no limits. When a study participant logs onto the website they will initially be asked questions which are aimed at identifying if their asthma could be better controlled. There will also be the ability to navigate to other self help areas within the site. The researchers agreed that the site will partly be educational but also the tone will challenge the users’ beliefs to promote better individual asthma control.

2. The Committee asked if the website would not be fully developed before making it available to patients. Professor Mair explained that focus groups involving volunteers from Asthma UK are currently involved in the development of the website as a piloted website.

3. The Committee asked why the invitation would be sent by the GP Practice as they felt that this could influence the potential participants to take part in the study. Professor Mair explained that this approach is common practice within Primary Care.

4. The Committee asked how the researchers will ensure that all inclusion and exclusion criterion are adhered to and you explained that a list of potential participants will be prepared in each GP Practice and then these will be manually checked by someone in the GP Practice to ensure that the patients to be contacted meet the inclusion and exclusion criteria.
5. The Committee asked what "website access" will be given to participants in the study, as stated in the Participant Information Leaflet. You explained that this means that people who are in the Control Group who do not have a log-on to the website, but will be given a log-on to allow them to access the website for 12 weeks.

The Committee is unable to give an ethical opinion on the basis of the information and documentation received so far. Before confirming its opinion, the Committee requests that you provide the further information set out below.

Authority to consider your response and to confirm the Committee’s final opinion has been delegated to a meeting of the sub-committee of the REC.

Further information or clarification required

1. The Committee had significant concerns arising from a lack of information about the nature of the on-line material and how it might operate for any particular patient. The Committee therefore requested more information, including screen capture(s) of how the online asthma self management resource will appear and work.

2. With regard to recruitment, the Committee decided that a potential participant who does not respond to the initial approach from the GP must not be contacted again by the researchers.

3. In the IRAS application form, QA17-1, it is stated that the Juniper Asthma Control Questionnaire will be used to establish as an inclusion criteria. As this was not submitted as part of the application the Committee would like to see this.

4. In the Participant Information Leaflet, section headed "What will happen to me if I take part?", second paragraph, give a clear explanation as to what website access for 12 weeks means, i.e. a log-on for the website for 12 weeks and not a computer or internet access.

If you would find it helpful to discuss any of the matters raised above or seek further clarification from a member of the Committee, you are welcome to contact Evelyn Jackson, contact details above.

When submitting your response to the Committee, please send revised documentation where appropriate underlining or otherwise highlighting the changes you have made and giving revised version numbers and dates.

If the committee has asked for clarification or changes to any answers given in the application form, please do not submit a revised copy of the application form; these can be addressed in a covering letter to the REC.

The Committee will confirm the final ethical opinion within a maximum of 60 days from the date of initial receipt of the application, excluding the time taken by you to respond fully to the above points. A response should be submitted by no later than 22 February 2013.
Membership of the Committee

The members of the Committee who were present at the meeting are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

13/WS/0004 Please quote this number on all correspondence

Yours sincerely

[Signature]

For Dr Brian Neilly
Chair

Enclosures: List of names and professions of members who were present at the meeting and those who submitted written comments.

Copy to: Dr Maureen Travers, R&D Office, Tennent Building, Western Infirmary
West of Scotland
REC 4

Attendance at Committee meeting on 11 January

2013 Committee Members:

<table>
<thead>
<tr>
<th>Name</th>
<th>Profession</th>
<th>Present</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ms Lynda Brown</td>
<td>Public Health Adviser</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Dr Andrew Clark</td>
<td>Consultant Haematologist</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Ms Cristina Coelho</td>
<td>Pharmacist</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Dr Clair Evans</td>
<td>Consultant Paediatric and Perinatal Pathologist</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Dr Kenneth James</td>
<td>Consultant Anaesthetist</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Dr Grace Lindsay</td>
<td>Reader</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Miss Fiona Mackelvie</td>
<td>(Retired) Lay member</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Ms Margaret McDonald</td>
<td>Retired (Lay Member)</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Mrs Cynthia Mendelsohn</td>
<td>Retired (Lay member)</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Dr Brian Neilly (Chair)</td>
<td>Consultant Physician</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Dr Jackie Riley</td>
<td>Statistician</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Dr Ihab Shaheen</td>
<td>Consultant Paediatric Nephrologist</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Mrs Kathleen Tuck</td>
<td>Retired Teacher</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Mr Iain Wright</td>
<td>Consultant Engineer (Lay member)</td>
<td>Yes</td>
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</tbody>
</table>

Also in attendance:

<table>
<thead>
<tr>
<th>Name</th>
<th>Position (or reason for attending)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Judith Godden</td>
<td>Scientific Adviser</td>
</tr>
<tr>
<td>Ms Evelyn Jackson</td>
<td>Committee Co-ordinator</td>
</tr>
<tr>
<td>Ms Linda Renfrew</td>
<td>Consultant Physiotherapist in MS Observer</td>
</tr>
</tbody>
</table>

Written comments received from:

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mrs Cynthia Mendelsohn</td>
<td>Retired (Lay member)</td>
</tr>
</tbody>
</table>
Dear Dr Neilly,

Study Title: A pilot Randomised Controlled Trial of Asthma Internet Self Management Intervention. The RAISIN Study.

REC reference: 13/WS/0004
Protocol number: GN12RM562
IRAS project ID: 120011

Many thanks for your correspondence following our attendance at the WOS REC 4 meeting on the 11th January 2013. From your letter you highlighted four main areas requiring consideration. These are answered in turn below.

“1. The Committee had significant concerns arising from a lack of information about the nature of the on-line material and how it might operate for any particular patient. The Committee therefore requested more information, including screen capture(s) of how the online asthma self management resource will appear and work.”

We appreciate your concerns about this lack of information. Attached to this letter are word documents and section showing screen shots of how the website will appear. We cannot yet provide a link to the website as it is still under construction but the attached documents provide examples of typical content of sections that will be available to participants in the remaining think aloud studies, and subsequently the trial. The enclosed contents should allow members of the Committee to get a feel for what the website will be like. Any changes to this content, or additional material, will be reviewed by our expert panel prior to inclusion in the website. This panel is:

1) Professor Neil Thomson, Consultant Respiratory Physician, University of Glasgow
2) Professor Frances Mair, GP and primary care researcher, University of Glasgow
3) Professor Sally Wyke, social scientist, University of Glasgow
4) Professor Mike Thomas, GP, primary care researcher & Chief Medical Officer at Asthma UK, University of Southampton
5) Professor Lucy Yardley, Health Psychologist, University of Southampton
6) Dr Deborah Morrison, GP and primary care researcher, University of Glasgow

Of note we have completed 3 ‘think aloud’ studies since the meeting on the 11th January using the material provided and user feedback has been very positive.

In addition we have been fortunate enough to be allowed to link to another LifeGuide website aimed at facilitating smoking cessation with our asthma resource.\(^1,2\) If users click on the link “Like to stop smoking?” they will be directed to this online intervention which has already been piloted with positive results so far.\(^3\) A demonstration version of this is freely available to view by clicking on the link or copying and pasting it into a web browser: http://www.lifeguideonline.org/player/play/stopadvisor demonstation?thiz=welcomerc

“2. With regard to recruitment, the Committee decided that a potential participant who does not respond to the initial approach from the GP must not be contacted again by the researchers.”

We would respectfully ask the Committee to reconsider this requirement because: 1) as we explain below we have genuine concerns that a single mailing will not allow us to achieve our recruitment target (and we provide below evidence to substantiate this assertion); 2) it is considered standard practice to contact potential participants a second time and there are many examples of this in the literature,\(^3-6\) and also with the first phase of this project (REC no 12/WS/0068) and 3) establishing recruitment rates is an important outcome of this pilot study, and being able to report response rates to initial mailings, second mailings and telephone contact will be an important finding in itself, and will inform the protocol of any future RCT that will stem from this work.

Our main concern about not reaching recruitment targets with a single mailing is based on experience at the Asthma Research Unit at Gartnavel General Hospital. We have experience of recruiting adults with asthma from primary care to RCTs which confirms how challenging it can be.\(^7-9\) Our experience is in keeping with the evidence base around the difficulties of recruitment.\(^10-12\) Recent positive response rates for trials conducted by our group (which include second mailings, and telephone reminders) have been poor ranging from 9-16% (See enclosed Table 1). Furthermore, based on our earlier experience, only 25-55% of those who respond positively will fulfil our inclusion criteria and be randomised. Thus, we know that recruitment will be challenging and based on our prior trials do not believe that a single mailing will yield sufficient participants. This was the case for the recent asthma RCT\(^8\) (Table 1, trial 3) where second mailings, and reminder telephone calls were then utilised to successfully meet targets. These strategies had been approved at the initial REC submission stage (REC no 09/S0703/23), allowing them to be operationalised as soon as poorer than expected recruitment was identified, and was considered key to it achieving targets.

We would however, be content to modify our protocol so that we ask for permission to write to non-responders a second time, OR to follow up with a telephone call reminder,
rather than do both as was requested in our initial application. We would also give potential participants explicit opportunity to opt out of being contacted a second time.

This is via a modification to the reply slip v1.0 which currently states:

I cannot or do not wish to participate in this study.
Name__________________________________________________
GP surgery_____________________________________________
(This is so we do not contact you again about this study)

This section of the document could be reworded (reply slip v1.1) to read:

I cannot or do not wish to participate in this study. Please do not contact me again.
Name__________________________________________________
GP surgery_____________________________________________
(We may contact those who don’t respond to the initial mailing one further time either by telephone or by post).

We hope that by explaining why we feel these measures are necessary, and giving potential participants explicit opportunity to opt out of a second contact you will reconsider your stance on this issue.

“3. In the IRAS application form, QA17-1, it is stated that the Juniper Asthma Control Questionnaire will be used to establish as an inclusion criteria. As this was not submitted as part of the application the Committee would like to see this.”

The Committee have pointed out that question A17-1 appears to refer to an additional patient measure ‘Juniper Asthma Control Questionnaire (6 question version)’. This is the same as the Asthma Control Questionnaire (ACQ) which was submitted with the initial application, but without the final 7th question. This 7th question requires a measure of lung function, and this will only be done if the participant is included in the study.

Therefore at telephone screening the first 6 questions will be asked to determine if a baseline visit is warranted. If, at the baseline visit inclusion criteria are fulfilled, then part of this visit includes a measure of lung function which will allow us to record the full 7 question ACQ score.

The term Juniper is sometimes used to describe the questionnaire as it was developed by Prof Elizabeth Juniper.
We apologise that it was not made sufficiently clear in our initial application that these measures were both referring to the same questionnaire set.

“4. In the Participant Information Leaflet, section headed “What will happen to me if I take part?”, second paragraph, give a clear explanation as to what website access for 12 weeks means, i.e. a log-on for the website for 12 weeks and not a computer or internet access.”

Many thanks to the Committee for highlighting this area of possible confusion to potential participants. The line in participant information sheet v1.0 (date 13/12/12):

“If you didn’t have website access you will be given it now for 12 weeks.”

has been replaced by:

“If you were in the group not using the website, you will be given a login now to access the website for 12 weeks.”

in the updated participant information sheet v1.1 (date 12/02/13).

Please find below a list of the documents enclosed with this letter:

<table>
<thead>
<tr>
<th>Appendix</th>
<th>Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Web section: Introduction and goal setting</td>
</tr>
<tr>
<td>B</td>
<td>Web section: My asthma sections example “I have never used a preventer inhaler”</td>
</tr>
<tr>
<td>C</td>
<td>Web section: SCREENSHOT Annual review (in powerpoint form to illustrate web appearance)</td>
</tr>
<tr>
<td>D</td>
<td>Web section: Physical activity and asthma</td>
</tr>
<tr>
<td>E</td>
<td>Web section: Common Concerns and Queries</td>
</tr>
<tr>
<td>F</td>
<td>Web section: Stress and Anxiety</td>
</tr>
<tr>
<td>G</td>
<td>Web section: Take the 4 week challenge</td>
</tr>
<tr>
<td>H</td>
<td>Web section: Action plans</td>
</tr>
<tr>
<td>I</td>
<td>Example email contents (to those who haven’t opted out, approximately 2 monthly)</td>
</tr>
<tr>
<td>J</td>
<td>Participant information Sheet v1.1 date 12/2/13</td>
</tr>
<tr>
<td>K</td>
<td>Participant reply slip v1.1 date 14/2/13</td>
</tr>
<tr>
<td>L</td>
<td>Table 1 – Examples of asthma trial recruitment</td>
</tr>
</tbody>
</table>

Many thanks for the opportunity to respond to your concerns and queries. If you would like any further information please do not hesitate to get in touch. I look forward to hearing your response.

Yours sincerely,

Dr Deborah Morrison                  Prof Frances S Mair

Institute of Health & Wellbeing

General Practice & Primary Care, 1 Horselethill Road, Glasgow. G12 9LX
Deborah.Morrison@glasgow.ac.uk
0141 330 8383

The University of Glasgow, charity number SC004401
Reference List


Ref Type: Unpublished Work


Dear Dr Morrison

<table>
<thead>
<tr>
<th>Study title:</th>
<th>A pilot Randomised Controlled Trial of Asthma Internet Self Management Intervention. The RAISIN Study</th>
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<td>Protocol number:</td>
<td></td>
</tr>
<tr>
<td>IRAS project ID:</td>
<td>120011</td>
</tr>
</tbody>
</table>

Thank you for your letter of 22 February 2013, responding to the Committee’s request for further information on the above research and submitting revised documentation.

The further information was considered, in correspondence by a sub-committee of the REC. A list of the sub-committee members is attached.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the Co-ordinator Ms Evelyn Jackson, evelyn.jackson@ggc.scot.nhs.uk.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation, as revised, subject to the conditions specified below.
Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

*Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.*

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at [http://www.rdforum.nhs.uk](http://www.rdforum.nhs.uk).

*Where a NHS organisation’s role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.*

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

*Sponsors are not required to notify the Committee of approvals from host organisations.*

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

<table>
<thead>
<tr>
<th>Document</th>
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<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
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<tr>
<td>Protocol 1.1</td>
<td>1.1</td>
<td>13 December 2012</td>
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<td>Investigator CV</td>
<td>-</td>
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<tr>
<td>Letter of invitation to participant 1.0</td>
<td>1.0</td>
<td>13 December 2012</td>
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<td>Participant Information Sheet</td>
<td>1.1</td>
<td>12 February 2013</td>
</tr>
<tr>
<td>Participant Consent Form</td>
<td>1.0</td>
<td>13 December 2012</td>
</tr>
</tbody>
</table>
## Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

### After ethical review

### Reporting requirements

The attached document “After ethical review – guidance for researchers” gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

### Appendix 11 Research Ethics Committee correspondence

<table>
<thead>
<tr>
<th></th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP/Consultant Information Sheets</td>
<td>13 December 2012</td>
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<tr>
<td>Evidence of insurance or indemnity</td>
<td>08 August 2012</td>
</tr>
<tr>
<td>Interview Schedules/Topic Guides</td>
<td>13 December 2012</td>
</tr>
<tr>
<td>Advertisement</td>
<td>13 December 2012</td>
</tr>
<tr>
<td>Other: Reply slip</td>
<td>13 December 2012</td>
</tr>
<tr>
<td>Other: Letter to GP confirming patient participation</td>
<td>13 December 2012</td>
</tr>
<tr>
<td>Other: Letter from funder(CSO)</td>
<td>21 June 2011</td>
</tr>
<tr>
<td>Other: Letter from CSO(Dr Elaine Moir)</td>
<td>23 May 2011</td>
</tr>
<tr>
<td>Other: Academic Supervisor CV - Prof FMair</td>
<td>-</td>
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<tr>
<td>Other: Academic Supervisor CV - Prof S Wyke</td>
<td>-</td>
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<tr>
<td>Other: Academic Supervisor CV - Emeritus Prof NC Thomson</td>
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<tr>
<td>Other: Academic Supervisor - Dr AMcConnachie</td>
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<tr>
<td>Other: CV - Karolina Agur</td>
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<td>Other: Web Sections x 8</td>
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<tr>
<td>Other: Example email contents</td>
<td>-</td>
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<tr>
<td>Other: Participant Reply Slip</td>
<td>14 February 2013</td>
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<tr>
<td>Other: Examples of asthma trial recruitment</td>
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<tr>
<td>Questionnaire: Asthma Control Questionnaire(ACQ)</td>
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<td>Questionnaire: Mini Asthma Quality of Life Questionnaire(MiniAQLQ)</td>
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<tr>
<td>Questionnaire: Patient Activation Measure</td>
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<tr>
<td>Questionnaire: EQ-5D</td>
<td>-</td>
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<tr>
<td>Questionnaire: Morisky Medication Adherence Scale</td>
<td>-</td>
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<tr>
<td>Questionnaire: Problematic Experience of Therapy Scale(PETS)</td>
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<tr>
<td>Referees or other scientific critique report</td>
<td>03 May 2011</td>
</tr>
<tr>
<td>Response to Request for Further Information</td>
<td>22 February 2013</td>
</tr>
</tbody>
</table>
The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

<table>
<thead>
<tr>
<th>13/WS/0004</th>
<th>Please quote this number on all correspondence</th>
</tr>
</thead>
</table>

We are pleased to welcome researchers and R & D staff at our NRES committee members’ training days – see details at [http://www.hra.nhs.uk/hra-training/](http://www.hra.nhs.uk/hra-training/)

With the Committee’s best wishes for the success of this project.

Yours sincerely

For Dr Brian Neilly
Chair

Enclosures: List of names and professions of members who were present at the meeting and those who submitted written comments
“After ethical review – guidance for researchers”

Copy to: Dr Maureen Travers, R&D Office, Tennent Building, Western Infirmary

West of Scotland REC 4

Participation in the Sub-Committee of the REC meeting held in correspondence

<table>
<thead>
<tr>
<th>Name</th>
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<td></td>
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<tr>
<td>Dr Brian Neilly (Chair)</td>
<td>Consultant Physician</td>
<td></td>
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</tr>
</tbody>
</table>

Appendix 11 Research Ethics Committee correspondence
Amendment 01 - summary of changes requested, submitted via IRAS online form 11th April 2013.

There are 4 areas requiring review.

1. Change to the section ‘Assessment and Reporting of Adverse Events’ found on page 24 of Protocol v1.1. This should be replaced with the updated version, as shown in Protocol v2.0. The wrong version was inadvertently sent in our initial application, and we apologise for this.

2. Reduced use of the Problematic Experiences of Therapy Scale (PETS) than originally described. In Protocol v1.1, (pages 7 & 14), the PETS is listed as a questionnaire which is carried out at baseline and follow up by both groups. However this questionnaire is actually only completed once, by participants in intervention group, at the followup visit. It is a measure of how easy or difficult they found using the website. The use of PETS is correctly described in the original study flow chart.

3. Change to wording of the PETS to make it more specific to this study. In consultation with the team who developed this scale, we have a version which is more appropriate to use when evaluating a website. In summary this involves changing the wording within questions from ‘skipped the therapy’ to ‘did not use/follow the Asthma website advice’, and from ‘carrying out the therapy’ to ‘use/follow the Asthma website advice’. There is no change to the actually underlying meaning of the question being asked. Full details of the changes are attached. Relevant documents: i. Original PETS questionnaire ii. New proposed version iii. Table showing changes to individual questions for comparison.

4. Incorrect questionnaire listed in IRAS questions A11 and A58. It lists the Knowledge, Attitudes and Self Efficacy Questionnaire (KASEEQ) where it should list the Patient Activation Measure (PAM). The PAM is correctly listed in the original protocol v1.1, and was correctly submitted as supporting documents with the original application; however I apologise for omitting to correct the IRAS forms in these two instances.
Dear Dr Morrison

Study title: A pilot Randomised Controlled Trial of Asthma Internet Self Management Intervention. The RAISIN Study.

<table>
<thead>
<tr>
<th>REC reference:</th>
<th>13/WS/0004</th>
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<tr>
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<td>AM01</td>
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<tr>
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<tr>
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<td>08 April 2013</td>
</tr>
<tr>
<td>IRAS project ID:</td>
<td>120011</td>
</tr>
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</table>

The above amendment was reviewed at a meeting of the Sub-Committee, held in correspondence.

**Ethical opinion**

The members of the Committee taking part in the review gave a favourable ethical opinion of the following amendments on the basis described in the notice of amendment form and supporting documentation:

- Change to section “Assessment and Reporting of Adverse Events” of the protocol.
- Reduced use of the Problematic Experiences of Therapy Scale (PETS).
- Change to wording of the PETS.
- Incorrect questionnaire listed in IRAS form.

**Approved documents**

The documents reviewed and approved at the meeting were:
Appendix 1 Research Ethics Committee correspondence

<table>
<thead>
<tr>
<th>Document</th>
<th>Version</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protocol</td>
<td>2.0</td>
<td>28 March 2013</td>
</tr>
<tr>
<td>Notice of Substantial Amendment (non-CTIMPs)</td>
<td>AM01</td>
<td>08 April 2013</td>
</tr>
<tr>
<td>Covering Letter</td>
<td>-</td>
<td>09 April 2013</td>
</tr>
<tr>
<td>PETS original version</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Old and new version of SAE Assessment and Reporting</td>
<td>0.2</td>
<td>-</td>
</tr>
<tr>
<td>List of PETS question changes</td>
<td>-</td>
<td>-</td>
</tr>
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</table>

**Membership of the Committee**

The members of the Committee who took part in the review are listed on the attached sheet.

**R&D approval**

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

**Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members’ training days – see details at [http://www.hra.nhs.uk/hra-training/](http://www.hra.nhs.uk/hra-training/)

<table>
<thead>
<tr>
<th>Name</th>
<th>Profession</th>
<th>Capacity</th>
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<tbody>
<tr>
<td>Dr Ken James</td>
<td>Consultant Anaesthetist</td>
<td>Expert</td>
</tr>
<tr>
<td>Dr Brian Neilly (Chair)</td>
<td>Consultant Physician Expert</td>
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</tr>
<tr>
<td>Dr Jackie Riley</td>
<td>Statistician</td>
<td>Expert</td>
</tr>
</tbody>
</table>

Yours sincerely

[Signature]

*For Dr Brian Neilly*

*Chair*

*Enclosures: List of names and professions of members who took part in the review*

*Copy to: Dr Maureen Travers, R&D Office, Tennent Building, Western Infirmary West of Scotland REC 4*

List of names and professions of members who took part in the review
Dear <Patient name>,

We are writing to ask for your help with a study being undertaken by the Department of General Practice & Primary Care, at the University of Glasgow.

We are supporting this exciting study which aims to test a website which has been developed to help people with asthma learn about, and manage, their asthma better. The researchers are looking for people with asthma to test out the website to find out if it is helpful and useful to people like you.

A leaflet is enclosed which gives more details about what this would mean for you.

Please have a read of this, and if you have any questions then do not hesitate to contact the researcher involved – Dr Deborah Morrison – who is happy to answer any queries. The contact details are on the back of the leaflet. If you are interested simply post back the enclosed form in the reply paid envelope.

Yours sincerely,

<GP/Practice Name>
A pilot Randomised Controlled Trial of an Asthma Internet Self Management Intervention – The RAISIN Study.

I am interested in helping with this research

I have read the participant information sheet and I am interested to hear more about the study. Please contact me to discuss this further.

Name ........................................................................................................................................
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Telephone number ................................................................................................................

Email address ........................................................................................................................

Which is the best way to contact you? Telephone ☐ Email ☐

Please fill this in and send it back to the research team in the reply paid envelope, or scan and email it.
(Please keep the participant information sheet).

Alternatively contact the researcher, Deborah Morrison, directly by:

Email: deborah.morrison@glasgow.ac.uk or Telephone: 0141 330 8383

I cannot or do not wish to participate in this study. Please do not contact me again.

Name.................................................................................................................................

GP surgery..........................................................................................................................

(We may contact those who don’t respond to the initial mailing one further time either by telephone or by post).
To find out more about the study, or tell us that you are interested in taking part, please return the form in the reply paid envelope or contact:

Deborah Morrison
General Practice & Primary Care
Institute for Health and Wellbeing
1 Horselethill Road,
University of Glasgow, G12 9LX
Telephone: 0141 330 8383
Email: Deborah.Morrison@glasgow.ac.uk

This study is sponsored by:

This study is funded by:

If you have any concerns about the research:
Professor Graham Watt
General Practice & Primary Care
Institute for Health and Wellbeing
1 Horselethill Road,
University of Glasgow, G12 9LX
Telephone: 0141 330 8330

Information about the research
You are being invited to take part in a research study. Before you decide whether to take part it is important that you understand why the research is being done and what it will involve for you.

Please take some time to read the following information carefully. Feel free to discuss the study with family or friends before you decide.

Why have I been chosen?
GP's are helping us with our research by sending information about our study to adults aged 16 years of older with a diagnosis of asthma. Alternatively you may have seen a poster, or been handed this information sheet by another health professional.

Do I have to take part?
No, it is up to you to decide if you want to take part or not. Your current or future care will not be affected whether you decide to take part or not.
Why is the study being done?
People with asthma often put up with symptoms such as wheeze, shortness of breath or interrupted sleep without realising that adjusting their inhalers might help. Some studies have shown that people with asthma have fewer symptoms when they use websites to receive information and feedback about their symptoms and medications. We have developed a resource which aims to do this, which will be available free of charge. Before it can be made widely available we need to find out how it works in practice, which is why we are trying it out in a pilot study. We want to find out how the website is used so we can learn ways to improve it.

What will happen to me if I take part?
We will put people into two groups: one group will get to use the website for 12 weeks, and the other group will manage their asthma as normal. Each person is put into a group by chance.
If you agree to take part a researcher will visit you at home. We will collect some information about you and your health and medications, and also some breathing tests. These are straightforward and involve you blowing into a machine. You will then be randomly put to one of the two groups. Twelve weeks after the first visit we will visit you again and ask you similar questions, and check your lung function again. If you didn’t have website access you will be given it now for 12 weeks. We also want to interview some people about the views on using the website.

Do I need access to the internet to take part?
Yes, this is a requirement. However it does not need to be within your own home. If you visit the library regularly, or family/friends with internet then you could still be eligible.

Will I benefit from taking part?
The information gathered from this study should help to improve the future care of people with asthma. We don’t know yet if using this website will be of direct benefit to you—that is what we want to find out!

Could I come to harm by taking part?
This website aims to help people manage asthma better. It is important that if you are feeling unwell or your asthma is getting worse while you are in this study that you contact your GP or practice nurse as you would normally. If you do this we don’t see any risks to you taking part.

We will take up some of your time, approximately 60 minutes for each visit. In order to keep your personal information safe we will follow strict procedures, as below.

Will other people find out I am taking part in this study?
Other than your GP no one else will find out. We need to inform your GP that you are taking part. We have strict ethical and legal practices we must adhere to. All information which is collected about you during this study will be kept strictly confidential. Any information about you will have your identifiable details removed so you cannot be recognised.

What will happen to the results?
We will use the information from the study to write up reports. We will share the findings with other researchers and interested groups such as Asthma UK. These reports will not include any information which would allow you to be recognised. We can send you the results of the study if you are interested.

What do I do if I want to take part?
If you decide you might like to take part please fill out the reply form, and post it back in the reply paid envelope. If preferred phone or email the researcher (details overleaf).

What do I do if I don’t want to/cannot take part?
It would be helpful to us to fill out the reply slip and return it in the reply paid envelope.

Who is running the study?
The study is being conducted at the University of Glasgow. It is funded by the Chief Scientist Office (CSO) Scotland, and is sponsored by NHS Greater Glasgow & Clyde.
Supporting Self Care for Asthma

A Randomised controlled trial of an Asthma Internet Self care Intervention

We are testing a website for people with asthma & we would like your help!

If you are 16 years old or over and would like to find out more please contact:
Deborah Morrison on 0141 330 8383 or deborah.morrison@glasgow.ac.uk
1. It is XX from the asthma website study. Thank you for responding to the mailing, we appreciate you taking the time to do that. Is now a good time to have a quick it?
2. Firstly, can I ask you some questions about your own health and your asthma to check if you are eligible for the study. Then if you are, I will tell you what the study involves and you can see if you would be interested in helping out? Would that be okay?
3. Can I ask your age please? (Ask postcode if phoned in, rather than responded to mailing)
4. Do you have a diagnosis of asthma?
5. Do you have any other lung conditions, or have you been told you have COPD or chronic bronchitis?
6. Do you have the internet in your house?
7. Is this on a laptop or computer? (website doesn’t work on tablets and smartphones)
8. Have you been to hospital or the doctors for your asthma in the last month?
   (postpone rest of screening if:
   a) Been to A&E,GEMS, hospitalised for asthma in last 4 weeks
   b) Been given oral steroids for asthma in last 4 weeks
   c) Been to see GP or nurse because of a flare in symptoms in last 4 weeks.
      a. (it is okay if been for annual review only, or if had a bit of a flare of symptoms that didn’t need to see doc or nurse for).
9. Can I ask you some questions about your asthma now? ACQ……..
10. That all sounds fine from our point of view.
11. Can I tell you a little about the study just now?
    a. We have developed a website which we think will be of interest to people with asthma and we need people to try it out. If you agreed to take part we would come to your house, ask some more questions about your health and asthma and how it affects you. We would then do some simple breathing tests. If everything was okay we would then find out if you were to get the website now, which is the case for half of you, or whether you get it in 3 months time. If you are allocated to the website group we simply give you a login and you can use the website as much or as little as you like over the next 12 weeks. This first visit takes about one hour.
    b. We would then arrange to visit you again after 12 weeks and repeat some of the questions and the breathing tests. If you have been given the website we would also like to ask you some questions about what you thought of the website.
12. Does that sound like something you would be interested in helping out with? If yes…..
13. Is there a time of day or a day of the week which would suit you best to visit? We can be flexible. We can do early evenings some days of the week if that is better for you…..
14. I will drop you an email just now confirming the date and time, and then you can let us know if anything crops up that we need to re-arrange.
15. The other thing to mention is that we would ask you to not use your inhalers the day we visit. This is because it can affect the results of the breathing tests. However we do say to people that if you need them in particular your reliever inhaler then you just go on ahead and take it – we can always adjust for it if needs be. We don’t want anyone going into a full blown asthma attack because of us.
16. Please let us know if you have to see a doctor about your asthma between now and then as we will need to postpone the visit.
Appendix 15  Chronic conditions included in co-morbidity count

Conditions included for co-morbidity count

1. hypertension
2. cardiovascular
3. rhinitis (perennial or allergic)
4. eczema/psoriasis
5. musculoskeletal (covering osteoporosis, scoliosis, slipped disc)
6. chronic lung disease
7. anxiety
8. depression
9. liver disease
10. renal tract disease
11. epilepsy
12. dyspepsia/ulcer
13. dementia
14. allergic condition (oral allergy syndrome)
15. chronic neurological condition (e.g. cerebral palsy)

This list is not meant to be a comprehensive list of all chronic medical conditions. I listed all the medical conditions which our participants had (both from our list, plus those ‘free texted’) and grouped related ones together, and removed those not considered to be a chronic condition (e.g. resolved (pregnancy induced) hypertension)
A. EQ-5D Questionnaire

1. Describing your health TODAY

Under each heading, mark ONE box that best describes your health TODAY.

**Mobility** (walking about)
- I have no problems walking about
- I have some problems walking about
- I have a lot of problems walking about

**Looking after myself**
- I have no problems washing or dressing myself
- I have some problems washing or dressing myself
- I have a lot of problems washing or dressing myself

**Doing usual activities** (for example, going to school, hobbies, sports, playing, doing things with family and friends)
- I have no problems doing my usual activities
- I have some problems doing my usual activities
- I have a lot of problems doing my usual activities

**Having pain or discomfort**
- I have no pain or discomfort
- I have some pain or discomfort
- I have a lot of pain or discomfort

**Feeling worried, sad or unhappy**
- I am not worried, sad or unhappy
- I am a bit worried, sad or unhappy
- I am very worried, sad or unhappy
2. How good is your health TODAY.

We would like to know how good or bad your health is TODAY. This line is numbered from 0 to 100. 100 means the best health you can imagine.

Please mark an X on the line that shows how good or bad your health is TODAY.
A. Morisky Medication Adherence Scale (MMAS)

© Morisky Medication Adherence Scale (MMAS-8-Item). This is a generic adherence scale and the name of the health concern can be substituted in each question item.

You indicated that you are taking medication for your asthma. Individuals have identified several issues regarding their medication-taking behaviour and we are interested in your experiences. There is no right or wrong answer. Please answer each question based on your personal experience with your asthma medication.

1. Do you sometimes forget to take your asthma medicine?  

   Yes  No
   0   1

2. People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your asthma medicine?  

   Yes  No
   0   1

3. Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it?  

   Yes  No
   0   1

4. When you travel or leave home, do you sometimes forget to bring along your asthma medicine?  

   Yes  No
   0   1

5. Did you take your asthma medicine yesterday?  

   Yes  No
   0   1

6. When you feel like your asthma is under control, do you sometimes stop taking your medicine?  

   Yes  No
   0   1

7. Taking medication everyday is a real inconvenience for some people. Do you ever feel hassled about sticking to your asthma treatment plan?  

   Yes  No
   0   1

8. How often do you have difficulty remembering to take all your medications? Please tick

   Never/Rarely
   Once in a while
   Sometimes
   Usually
   All the time

© Morisky Medication Adherence Scale (8-Item)
A. Mini AQLQ

Please complete all questions by circling the number that best describes how you have been during the last 2 weeks as a result of your asthma.

IN GENERAL, HOW MUCH OF THE TIME DURING THE LAST 2 WEEKS DID YOU:

<table>
<thead>
<tr>
<th>Question</th>
<th>All of the Time</th>
<th>Most of the Time</th>
<th>A Good Bit of the Time</th>
<th>Some of the Time</th>
<th>A Little of the Time</th>
<th>Hardly Any of the Time</th>
<th>None of the Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Feel SHORT OF BREATH as a result of your asthma?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>2. Feel bothered by or have to avoid DUST in the environment?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>3. Feel FRUSTRATED as a result of your asthma?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>4. Feel bothered by COUGHING?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>5. Feel AFRAID OF NOT HAVING YOUR ASTHMA MEDICATION AVAILABLE?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>6. Experience a feeling of CHEST TIGHTNESS or CHEST HEAVINESS</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>7. Feel bothered by or have to avoid CIGARETTE SMOKE in the environment?</td>
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<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>8. Have DIFFICULTY GETTING A GOOD NIGHT’S SLEEP as a result of your asthma?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>9. Feel CONCERNED ABOUT HAVING ASTHMA?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>10. Experience a WHEEZE in your chest?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
</tbody>
</table>

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A. Mini AQLQ Cont.

IN GENERAL, HOW MUCH OF THE TIME DURING THE LAST 2 WEEKS DID YOU:

11. Feel bothered by or have to avoid going outside because of WEATHER OR AIR POLLUTION?

<table>
<thead>
<tr>
<th>All of the Time</th>
<th>Most of the Time</th>
<th>A Good Bit of the Time</th>
<th>Some of the Time</th>
<th>A Little of the Time</th>
<th>Hardly Any of the Time</th>
<th>None of the Time</th>
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</table>

HOW LIMITED HAVE YOU BEEN DURING THE LAST 2 WEEKS DOING THESE ACTIVITIES AS A RESULT OF YOUR ASTHMA?

12. STRENUOUS ACTIVITIES (such as hurrying, exercising, running up stairs, sports)

<table>
<thead>
<tr>
<th>Totally Limited</th>
<th>Extremely Limited</th>
<th>Very Limited</th>
<th>Moderate Limitation</th>
<th>Some Limitation</th>
<th>A Little Limitation</th>
<th>Not at all Limited</th>
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<td>7</td>
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</tbody>
</table>

13. MODERATE ACTIVITIES (such as walking, housework, gardening, shopping, climbing stairs)

<table>
<thead>
<tr>
<th>Totally Limited</th>
<th>Extremely Limited</th>
<th>Very Limited</th>
<th>Moderate Limitation</th>
<th>Some Limitation</th>
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14. SOCIAL ACTIVITIES (such as talking, playing with pets / children, visiting friends / relatives)

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<thead>
<tr>
<th>Totally Limited</th>
<th>Extremely Limited</th>
<th>Very Limited</th>
<th>Moderate Limitation</th>
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15. WORK-RELATED ACTIVITIES* (tasks you have to do at work)

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<th>Totally Limited</th>
<th>Extremely Limited</th>
<th>Very Limited</th>
<th>Moderate Limitation</th>
<th>Some Limitation</th>
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*If you are not employed or self-employed, these should be tasks that you have to do most days

DOMAIN CODE:

SYMPTOMS: 1, 4, 6, 8, 10
ACTIVITY LIMITATION: 12, 13, 14, 15
EMOTIONAL FUNCTION: 3, 5, 9
ENVIRONMENTAL STIMULI: 2, 7, 11

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**A. Patient Activation Measure (PAM)**

Below are some statements that people sometimes make when they talk about their health. Please indicate how much you agree or disagree with each statement as it applies to you personally by ticking your answer. Your answers should be what is true for you and not just what you think others want you to say.

<table>
<thead>
<tr>
<th></th>
<th>Disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Agree</th>
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We would like to know how easy or difficult it was for you to use/follow the website’s advice. We want to find out if it was difficult in any way for you to use/follow, and if so, what difficulties were.

### Problems due to symptoms

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
<th>Agree</th>
<th>Agree</th>
<th>Not Sure</th>
<th>Disagree</th>
<th>Disagree</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>I did not use/follow the Asthma Website advice because it made my symptoms worse.</td>
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<td>2</td>
<td>I was prevented from using/following the Asthma Website advice by severe symptoms.</td>
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<td>3</td>
<td>I could not use/follow the Asthma Website advice because it caused more symptoms.</td>
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### Problems due to uncertainty or doubts about the therapy

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
<th>Agree</th>
<th>Agree</th>
<th>Not Sure</th>
<th>Disagree</th>
<th>Disagree</th>
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</thead>
<tbody>
<tr>
<td>4</td>
<td>I could not use/follow the Asthma Website advice because I was unsure how to do it properly.</td>
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<td>5</td>
<td>I was unable to use/follow the Asthma Website advice because it was difficult to know what to do.</td>
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<tr>
<td>6</td>
<td>I did not use/follow the Asthma Website advice because I was not sure if it was helping.</td>
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<td>7</td>
<td>I did not use/follow the Asthma Website advice because it did not seem relevant to my symptoms and problems.</td>
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<td>8</td>
<td>I did not use/follow the Asthma Website advice because I was not convinced it was right for me.</td>
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### Practical Problems

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<th>Not Sure</th>
<th>Disagree</th>
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<tbody>
<tr>
<td>9</td>
<td>Lack of time prevented me from using/following the Asthma Website advice.</td>
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<td>It was not possible to find suitable opportunities to use/follow the Asthma Website advice.</td>
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<td>I was too busy to use/follow the Asthma Website advice.</td>
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<td>12</td>
<td>I found it difficult to remember to use/follow the Asthma Website advice.</td>
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