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Informal Carers of Stroke Survivors

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Abstract

Chapter 1 Caring is a part of life

Synopsis of chapter 1

Chapter 1 discusses why the need for help and support from another person may arise and covers related areas; the ageing of the population, trends in disability free life expectancy, health conditions associated with disability, long term care of people with disabling conditions, the need for informal care for another person, the historical roots of the word 'carer' and exposure to informal care and the effects on health of the care provider. Chapter 1 also presents the broad aims and objectives for this entire body of work.

Chapter 2 Is informal care giving independently associated with poor health? A population-based study.

Synopsis of Chapter 2

Chapter 2 focuses on the analysis of secondary data from the UK Census 2001 to quantify the magnitude of association between informal care and reported poor health in the UK population 2001. The main methods of data analysis are described. The binary logistic regression techniques are described along with the assumptions underlying the regression models. The results are presented and discussed.

Abstract

Background Providing informal care has been linked with poor health but has not previously been studied across a whole population. The aim of this study was to determine the association between informal care provision and self-reported poor health.

Method Data from the UK 2001 Census was used. The relationship between informal care giving and poor health was modelled using logistic regression,

adjusting for age, sex, marital status, ethnicity, economic activity and educational attainment.

Results Data on 44,465,833 individuals free from permanent sickness or disability was included. 5,451,902 participants (12.3%) reported providing informal care to another person. There was an association between provision of informal care giving and self-reported poor health; odds ratio 1.100, 95% CI 1.096- 1.103. This association remained after adjustment for age, sex, ethnic group, marital status, economic activity and educational attainment. The strength of association also increased with the amount of care provided (hours per week).

Conclusions Informal care giving is associated with poor health, particularly in those providing over 20 hours of care per week.

Chapter 3 The Glasgow Carers Cohort Study: informal care giving and risk of disease

Synopsis of Chapter 3

Chapter 3 presents the Glasgow Carers Cohort Study (GCCS). For presentation purposes Chapter 3 is split into several sections. The chapter opens with an introduction to the clinical condition of stroke including a description of the pathological and clinical definitions of stroke, the consequences of stroke, the challenges of living with stroke and the need for informal care for another person and finishes with the GCCS cohort study hypothesis and aims. The next section describes the GCCS study design, the study conduct and the data analysis. The results are presented and discussed.

Abstract

Background Adults with disability often require some form of assistance from informal carers. While being a carer can be a rewarding experience it is plausible that the demands of care-giving can result in ill health. The study of stroke survivors and their carers can inform this debate, as stroke is a leading cause of complex adult disability and many stroke survivors require input from

informal carers. The aim of this study was to assess the effects of providing informal care on a group of people who provide care to stroke survivors compared to not providing informal care to anyone.

Method This was a prospective, six month study of two cohorts, one cohort of people who provided informal care to stroke survivors (exposed to care giving) and an age and sex matched random sample of a non care giving reference group from a Greater Glasgow and Clyde Health Board General practice population for comparison (non exposed). Participants in both exposed and non exposed cohorts had to be at least 16 years of age, fluent in English and free from any informal care-giving activities in excess of 20 hours per week at enrolment. The primary outcome measure was incidence of perceived stress as measured by the Perceived Stress Scale (PSS). Secondary outcomes were psychological well being, psychosomatic symptoms and depression.

Results 28 people who were identified as potential informal carers of stroke survivors were enrolled in this study and 41 age-sex matched non exposed participants were enrolled. Over 6 months of observation, 36% (9/25) of the “exposed” care giving group and 5% (2/39) of the unexposed cohort had their first occurrence of stress (PSS score ≥ 23). Participants who were exposed to providing care had lower happiness scores, mean difference -5.7 (95%CI: -8.0 to -2.5). There was no difference between groups in psychosomatic symptoms; or depression score. After adjustment for age, sex and perceived stress at baseline, informal caring was associated with a raised perceived stress odds ratio 6.26 (95% CI: 0.94 to 41.41) but this was not statistically significant ($p = 0.058$).

Conclusions The results of this cohort study are not conclusive. Nevertheless, they provide stronger evidence than previous studies that exposure to providing informal care to stroke survivors affects levels of perceived stress and levels of psychological well-being.

Chapter 4 Incidence, prevalence and association between providing informal care to stroke survivors and depression: a systematic review and meta-analysis.

Synopsis of chapter 4

Chapter 4 focuses on the analysis and evaluation of the existing epidemiological literature on the putative association between informal care and depression. For presentation purposes, this chapter is divided into several sections. The first section describes the concepts and methods that are fundamental to the epidemiologic study of informal carers and the rationale for the systematic review and meta-analysis. The second section describes the diagnostic criteria for depression and criteria for the informal care exposure and the questions being addressed. The third section describes the methods of the systematic review including types of study design, the types of participants, types of interventions, types of outcome and types of study, searching for studies, selecting studies and collecting data, assessing risk of bias in included studies and includes a description of methods for statistically summarising the results from multiple studies. The final section presents the meta-analysis of the relevant studies. The results are presented and discussed.

Abstract

Background Reliable data on the incidence and prevalence of depression in people who provide informal care to stroke survivors are useful for helping inform clinical trials, plan stroke services, inform informal caregivers and stroke survivors and for the development of good public policy. However, data on the prevalence of depression are conflicting. Moreover, prevalence of depression in people who provide care survivors does not equate to a cause and effect relationship between provision of informal care to stroke survivors and depression.

Objectives This systematic review was undertaken to 1) obtain valid and precise estimates of the occurrence of depression in people who provide informal care to stroke survivors, 2) to assess whether existing studies provide evidence of an association between provision of informal care to stroke survivors and accepted definitions of depression and to and 3) to identify factors associated with the development of depression in people who provide care to stroke survivors.

Search methods The following electronic databases were searched: MEDLINE (1950 to October 2010), EMBASE (1980 to October 2010), CINAHL (1982 to October 2010), (AMED (Allied and Complementary Medicine) (1985 to October 2010), PsycINFO (1967 to October 2010) and eight other databases. In an effort to identify further published, unpublished and ongoing studies, conference proceedings and trials registers were searched, reference lists of relevant articles were scanned and researchers and authors in the field were contacted.

Selection criteria Studies were included if the focus was on; study participants as a provider of care to a stroke survivor living in the community, had no restrictions on admissible participants, had no restrictions on type of stroke patient, depression was measured using standard criteria and measures of occurrence of depression presented in a binary format (i.e., depressed/ not depressed). Types of epidemiologic study eligible included: cohort studies, case-control studies, including prevalent case-control studies and cross sectional studies, including prevalence studies.

Data collection and analysis Two review authors selected studies for inclusion, independently extracted data and assessed methodological quality. Estimates of pooled prevalence were calculated using inverse variance methods.

Results 19 studies were identified. 12 studies used a single cohort design and six studies used a cross sectional design. One study is ongoing and awaiting assessment. No cohort studies included a referent or comparator group of people who were unexposed to providing informal care. Data on prevalence of depression were available from 16 studies (1848 participants). No studies were identified that collected data on incidence of depression. No investigators reported including participants to cohort studies that were free of depression at the initial observation. The estimates of prevalence of depression are based on the number of people who scored above a clinical cut point on a self-report dimensional rating scale for depression. The overall pooled prevalence estimate calculated using the inverse variance method using a random effects model was slightly lower (28%, 95% CI 23%, 33%) than when the analysis was restricted to studies with an ideal design (30%, 95% CI 25%, 34%). The majority of studies lack a description of important characteristics that define the informal caregiver

population. Lack of a clear and unambiguous operational definition of informal care is common across studies.

Conclusions Estimates of prevalence of depression in people who provide care to informal stroke survivors are similar to those observed in community studies of the prevalence of depression. There is currently insufficient evidence from epidemiological studies to suggest an association between the provision of informal care and the development of depression.

Chapter 5 Non-pharmacological interventions for informal carers of stroke survivors

Synopsis of chapter 5

Chapter 5 focuses on the analysis and evaluation of the existing literature on the effects of non pharmacological interventions targeted towards people who provide informal care to stroke survivors. For presentation purposes, this chapter is divided into several sections. Section A describes the background and rationale for the systematic review. Section B describes the methods of the review including the types of participants, types of interventions, types of outcome and types of study, searching for studies, selecting studies and collecting data, assessing risk of bias in included studies, methods for analysing data and undertaking meta-analysis. Section C presents the meta-analysis of the relevant studies. The results are presented and discussed.

Abstract

Background A substantial component of care is provided to stroke survivors by informal caregivers. However, providing such care is often a new and challenging experience and has been linked to a number of adverse outcomes. A range of interventions targeted towards stroke survivors and their family or other informal caregivers have been tested in randomised controlled trials (RCTs).

Objectives To evaluate the effect of interventions targeted towards informal caregivers of stroke survivors or targeted towards informal caregivers and the care recipient (the stroke survivor).

Search methods The Cochrane Stroke Group Trials Register (last searched March 2011), the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 4, 2010); MEDLINE (1950 to August 2010), EMBASE (1980 to December 2010), CINAHL; (1982 to August 2010), AMED (1985 to August 2010), PsycINFO (1967 to August 2010) Science Citation Index (1992 to August 2010) and six other electronic databases were searched. In an effort to identify further published, unpublished and ongoing studies, conference proceedings and trials registers were searched, reference lists of relevant articles were scanned and researchers and authors in the field were contacted.

Selection criteria RCTs were included if they evaluated the effect of non-pharmacological interventions (compared with no care or routine care) on informal caregivers of stroke survivors. Trials of interventions were included if they delivered to stroke survivors and informal caregivers only if the stroke survivor and informal caregiver were randomised as a dyad. Studies which included stroke survivors and caregivers were excluded if the stroke survivors were the primary target of the intervention.

Data collection and analysis Two review authors selected studies for inclusion, independently extracted data and assessed methodological quality. Original data was sought from trialists. Interventions were categorised into three groups: support and information, teaching procedural knowledge/vocational training type interventions, and psycho-educational type interventions. The primary outcome was caregivers' stress or strain. Disagreements were resolved by consensus.

Results Eight studies, including a total of 1007 participants, met the inclusion criteria. The results of all the studies were not pooled because of substantial methodological, statistical and clinical heterogeneity. For caregivers' stress or strain no significant results were found within categories of intervention, with the exception of one single-centre study examining the effects of a 'vocational training' type intervention which found a mean difference between the intervention and comparator group at the end of scheduled follow-up of -8.67 (95% confidence interval -11.30 to -6.04, $P < 0.001$) in favour of the 'teaching procedural knowledge' type intervention group

Conclusions It was not possible to carry out a meta-analysis of the evidence from RCTs because of methodological, clinical and statistical heterogeneity. One limitation across all studies was the lack of a description of important characteristics that define the informal caregiver population. However, 'vocational educational' type interventions delivered to caregivers prior to the stroke survivor's discharge from hospital appear to be the most promising intervention. However, this is based on the results from one, small, single-centre study.

Chapter 6 Conclusions

Synopsis of Chapter 6

This chapter, after outlining the findings of the individual studies included in this thesis and how they fit into the broader literature, makes observations about the approach that has been taken and lessons learned, some with the benefit of hindsight, in order to inform future research work on informal carers. This chapter also examines the structure, purpose, limitations, use and misuse of the informal care epidemiological literature. The chapter finishes with recommendations for future research, clinical practice and policy.

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Preface

When I started this body of research, I knew very little about informal carers of stroke survivors either professionally or personally. My own mother cared for my elderly maternal grandfather who had had a stroke and a frail elderly maternal great aunt. But, other than that my own experience of informal carers is very limited. This turned out to be a considerable advantage. Even though my naïveté could have caused me problems, which it sometimes did, mostly it gave me a new, fresh and different perspective to the study of informal carers. I had few predetermined ideas about what I should expect to find. I chose not to use conventional wisdom about the effects of informal care as a guide, preferring instead to use the opportunity to think independently and critically, and to challenge existing ways of thinking about informal care.

Providing informal care to a loved one, friend or neighbour in illness, frailty or disability is part of the fabric of life, something that one in eight people will have to deal with at one or more points in their life. However, it is only fairly recently that the public, governmental and non governmental bodies, health and social care professionals and researchers have begun to take an interest in the effects that providing what is necessary for the health, well-being, maintenance and safety of another individual in ill health, frailty or disability may have on the welfare of the individual providing the care. Conventional wisdom is that providing informal care is depressing, burdensome, stressful, anxiety provoking, physically exhausting and any number of serious adverse health outcomes. There is no debate. Given that one in eight people are exposed to providing informal care and the number of people who require informal care is about to increase exponentially, surely we have a burgeoning public health problem on our hands?

The first indication that this body of research was not going to go as originally planned was when I came across what I believed to be an unbelievable epidemiological estimate - 35% to 50% of people who provide care to stroke survivors are depressed. How could that many people be depressed? How could they be depressed and still carry on providing care? Where had this evidence come from? Was it really true? If it was true, what could be done?

I have always been interested in research methods. I wanted to use this opportunity primarily to develop my understanding of the concepts and methods of epidemiology and with the issues that are fundamental to the discipline. The epidemiological study of people who provide informal care to others in ill health, frailty or disability provided the perfect opportunity.

The approach to this body of research has been straightforward. The uniqueness of this research, if any, is that standard epidemiological methods for assessing the effects of informal care as a potential causal characteristic (or exposure) have been applied. Exposure refers to both a behaviour (providing informal care) and to an intervention (e.g., psycho educational interventions). None of the methods used in this body of research are new, but none of them had ever been applied as rigorously before to the epidemiological study of people who provide informal care.

I have for the most part written this body of work for myself. I wanted to develop my own understanding and find my own way through the epidemiological study of informal carers. I have the most basic training in epidemiological methods and therefore have approached this subject matter as an enquirer rather than a specialist. It has been a journey of discovery. At times the journey has been difficult, lonely and frustrating but ultimately it has been hugely rewarding.

Acknowledgements

Firstly, I would like to thank my husband, John, and my children, Cameron, David and Annie for their endless love, encouragement, support, patience and understanding throughout my candidature. I know they will all be very happy to reclaim the kitchen table for its intended purpose. I would also like to thank my parents, Elizabeth and Frank, for their help and support throughout the research and writing of this thesis.

I would like to thank my principal supervisor, Peter Langhorne, for his intellectual guidance, inspiration, friendship and support. I wish to express my indebtedness to Christopher Weir, Lorraine Smith and David Stott who generously shared their thoughts, insights, knowledge and criticisms with me, for providing comments on draft manuscripts and for their expertise, time, encouragement and friendship. I am especially grateful to Christopher Weir for his advice on statistics and for his wonderful approach; *suaviter in modo, fortiter in re*. Other people I wish to thank are Maree Hackett (Australia) for her advice on depression and Peter Cummings (University of Washington) for his advice on matching in cohort studies, Daniel L Segal (University of Colorado) for generously providing data from his study on psychometric properties of the Beck Depression Inventory-II (BDI-II) among community-dwelling older adults, which allowed me to calculate the clinical cut point for the Perceived Stress Scale for the cohort study, Graham Ellis for coming up with the idea of informal caregivers as a subject area for research and Terry Quinn for his encouragement, advice, friendship and hard work as a co-reviewer.

I wish to acknowledge the opportunity afforded me by the Chief Scientist Office, The Scottish Government, without whose commitment to my research training and financial support, this thesis would not have been possible.

I also wish to thank the academics whose books and papers I have read and courses I have attended. I have the deepest admiration for the scholars in the field of epidemiology, systematic reviews and statistics.

Finally, I would like to express my gratitude to all the people who provide care to stroke survivors who agreed to participate in my cohort study and all the people who volunteered to participate as members of the non-care giving reference group. Without them, there would be no study.

Author's Declaration

Chapter 1: The need for informal care

I was responsible for the literature review and I wrote the chapter.

Chapter 2: Is informal care giving independently associated with poor health? A population-based study

I was responsible for the study design, the study conduct, and the data analysis. I conceived the idea for the study, secured the funding, obtained the public sector information licence (PSI Licence C200900034) and wrote the chapter. I was responsible for the data cleaning, checking and coding.

Dr Linda De Caestecker, Director of Public Health and Allan Boyd, senior analyst/ Public Health, of Great Glasgow and Clyde Health Board for enabling the initial discussions with the Office for National Statistics (ONS).

Chapter 3: The Glasgow Carers Cohort Study: informal care-giving and risk of disease

I conceived and designed the research. I was responsible for the study design, the study conduct, the data analysis and writing up. This included seeking ethics approval and co-ordination of recruitment of participants. I designed the questionnaires, acquired the data, analyzed and interpreted the data, and performed all the statistical analysis.

The Scottish Stroke Research Network assisted with the recruitment of informal carers and the Scottish Primary Care Research Network assisted with the recruitment of non exposed participants from a general practice.

I designed the database for storing study data and analysing study data. Cameron Legg was responsible for entering the study data. I was responsible for cleaning, checking and coding study data.

Professor Peter Cummings, Emeritus professor of epidemiology at the University of Washington provided advice on matching in cohort studies and analysis of cohort studies. Professor Daniel L. Segal, professor of psychology at the University of Colorado at Colorado Springs provided data from his study on the psychometric properties of the Beck Depression Inventory-II (BDI-II) among community-dwelling older adults which enabled the calculation of the clinical cut-point for the Perceived Stress Scale. Dr Philip Cotton, academic director of vocational studies, section of general practice & primary care, University of Glasgow facilitated the involvement of the Primary Care Research Network for the recruitment of non care-giving participants from general practice. Dr Daniel McGhee, general practitioner, Townhead Health Centre, Glasgow allowed his practice to be used as the sampling framework for recruitment of non-care giving participants.

Chapter 4: Incidence, prevalence and association between providing informal care-giving to stroke survivors and depression, and factors associated with depression: a systematic review and meta-analysis.

I conceived and designed the research. I was responsible for the study design, the study conduct, the data analysis and writing up. I was responsible for running the search strategy, designing the data abstraction forms, acquiring the data, analyzing and interpreting the data and performing all the statistical analysis. I co-ordinated the co-reviewers work.

Dr Maree Hackett, senior research fellow at The George Institute for International Health, Sydney, Australia, provided advice on depression. Dr Terence J Quinn and Dr Christopher Weir acted as co-reviewers.

Chapter 5: Non pharmacological interventions for informal carers of stroke survivors

I conceived the idea for the review and designed the systematic review protocol. Jayne Teirney contributed to the planning of the analysis. I wrote the protocol. Brenda Thomas (Trials Search Co-ordinator for the Cochrane Stroke Group) designed the search history. I was responsible for running the search strategy,

designing the data abstraction forms, acquiring the data, analyzing and interpreting the data, performing all the statistical analysis and writing up.

Terry Quinn, Fahd Mahmood, Jayne Tierney, David Stott, Lorraine Smith and Peter Langhorne all participated in the assessment of risk of bias of each study and the classification of each study's intervention. Terry Quinn, Fahd Mahmood and Peter Langhorne acted as co-reviewers.

I wrote the first draft of papers that have been presented from this thesis. To date, the following chapters have either been accepted for publication or are going through the editorial process.

- 'Non-pharmacological interventions of informal carers of stroke survivors' has been accepted for publication in the Cochrane Library.
- 'Is informal care giving independently associated with poor health? A population-based study' is currently going through the editorial process at the Journal of Epidemiology and Community Health.

I have also received additional grant funding as a direct output from the findings in this thesis. Research grants have been awarded from NHS Greater Glasgow and Clyde Research Endowment Fund and the Robert Mairs Charitable Trust.

Definitions/Abbreviations

BDI	Beck Depression Inventory
CCI	Charlson comorbidity index
CES-D	Center for Epidemiologic Depression Scale
GDS	Geriatric Depression Scale
GGCS	Glasgow Carers Cohort study
HADS	Hospital Anxiety and Depression Scale
HRQOL	Health related quality of life
IDA	Irritability Depression-Anxiety Scale
MD	Mean difference
OHQ	Oxford Happiness Questionnaire
PSS	Perceived Stress Scale
PHQ	Patient health questionnaire
Rand SF 36	RAND 36-Item Health Survey 1.0
RD	Risk difference
RR	Risk ratio
SMD	Standardised mean difference

Chapter 1 Caring is a part of life

1.1 Introduction

1.1.1 The need for help or protection from another person

‘The reasons people might need help can vary. Maybe they were born with a disability or had an accident that left them disabled. Or they have an illness or disease. Their problems may be physical or mental. They might need help because they are getting older and frail. But what doesn't vary is that they need help, and if you look after someone - for whatever reason - caring is part of life.’

Carers.org. UK 2011.

For the purpose of this body of work informal care is defined as providing what is necessary for the health, welfare, maintenance or protection of another person in illness, frailty or disability. The need for informal care from another person can arise from: chronic diseases associated with ageing, chronic health conditions that have the potential to cause disability in childhood, injury related disability or other health conditions associated with disability.

1.1.2 An ageing population

The age structure of the population is shifting as a consequence of a combination of declining birth rates and increasing life expectancy, with more people living into old age¹. For example life expectancy for men and women in the United Kingdom (UK) has doubled in the last two hundred years. In 1851, the Victorian era, life expectancy at birth in England and Wales was 40.2 years for men, 42.2 for women. More than 70 per cent of the population were under 35. Out of every 1,000 babies, 150 died before they were one year old².

In 1901, males born in the UK life expectancy at birth was 45.0 years for males and 48.7 years for females. However, since 1901, life expectancy has risen by more than 30 years. Males born in 2008 can expect to live to 77.8 years compared with 81.9 years for females³. This increase in life expectancy has caused a 31 per cent increase in the proportion of over 65s in the population from 7.4 million in 1971 to 9.7 million in mid-2006 and a simultaneous 19 per cent decline in the population aged under 16, from 14.2 to 11.5 percent⁴. Historically, substantial increases in life expectancy have been driven by reductions in infant and neonatal mortality (*defined as deaths in the first year of life and deaths of babies fewer than 28 days old respectively*)^{1;3;5}. However, over the last forty years, while birth rates have declined, life expectancy has increased, mainly as a consequence of significant improvements in survival at older ages¹. However, the trend in increased survival into old age varies across Europe¹. Moreover, it is predicted that the life expectancy will continue to increase and the population of Europe will continue to age as a consequence of the age structure of people who are alive at the present time and of the long-term effects of the post Second World War and 1960s baby boom^{1;6}.

The risk of developing musculoskeletal disorders (such as arthritis and rheumatism), heart and circulatory disorders (such as heart attack or stroke), and many other chronic diseases increases with age³, as does the probability of disability caused by these chronic health conditions⁷. However, health conditions with higher prevalence (e.g., musculoskeletal conditions) have a reasonably low risk of disability compared to less prevalent conditions such as traumatic spinal cord injury or traumatic brain injury which have a high risk of associated disability⁷.

1.1.2.1 Disability free life expectancy

Disability-free life expectancy (DFLE), defined as the length of time that a person can expect to live free from a limiting long-standing illness or disability⁸, is decreasing with the proportion of persons reporting long-

standing illness increasing from 21 per cent in 1972 to 33 percent in 2005⁹. The age-adjusted rate for males aged 15-44 reporting a long-standing illness or disability is 175 per 1000 increasing to 554 per 1000 aged 65-74 and to 582 per 1000 aged 75 and above. The trend was similar for females; however, the highest rate for females reporting long-standing illness was 589 per 1000 in the 65-74 age group¹⁰. Therefore, while life expectancy has increased substantially, healthy life expectancy based on a summary of self-assessed general health or self-assessed limiting long-term illness, is less impressive¹¹. Therefore there has been a small increase in the number of years an individual can expect to spend with moderate disability or chronic illness.

People aged 65 and over are more likely to report long-standing illness³. For younger adults aged 16 - 44, respiratory problems are the most frequently reported cause of chronic sickness (with asthma affecting 29 per 1,000 men and 47 per 1,000 women) followed by back problems (affecting 21 per 1,000 men and 18 per 1,000 women). For middle-aged aged adults 45-64, arthritis and rheumatism were the most frequently reported cause of chronic sickness (affecting 114 per 1,000 males and 97 per 1,000 females) followed by other heart complaints for males (50 per 1,000) and asthma for females (45 per 1,000). For older adults (65 - 74) musculoskeletal problems (with arthritis and rheumatism affecting 114 per 1,000 men and 193 per 1,000 women) were the most commonly reported long standing illness. This was followed by other heart complaints (affecting 110 per 1,000 men) and other bone and joint problems for women (67 per 1,000). For very old adults aged 75 the most frequently reported cause of chronic sickness was musculoskeletal problems with arthritis and rheumatism affecting 118 per 1,000 men and 236 per 1,000 women, followed by other heart complaints (117 per 1,000 men and 111 per 1,000 women)³.

The proportion of persons reporting limiting long-standing illness also increased from 15 percent in 1972 to 20 percent in 2005⁹. The proportion of persons reporting limiting long-standing illness also increases with age.

The age-adjusted rates for males and females were highest in the 75 and over age group at 401 per 1000 and 402 per 1000 respectively compared to 90 per 1000 for males and 114 for females in the 15-44 age group¹⁰.

Musculoskeletal disorders are the most common reported cause of severe disability in the UK¹³. However, the proportion of severe disability among stroke survivors is twice as great as that reported by those suffering from musculoskeletal disorders (65% vs. 33%). Those with stroke have the highest odds of reporting more severe disability OR 4.88 (95% CI 3.79-6.29) followed by mental disorders OR 4.57 (95% CI 3.87-5.39) and then musculoskeletal disorders OR 2.75 (95%CI 2.48-3.06)¹³.

1.1.3 Other health conditions associated with disability

1.1.3.1 Health conditions associated with disability in childhood

Examples of clinical disorders and diseases associated with disability in childhood include: hereditary disorders such as tuberous sclerosis or muscular dystrophy; early alterations of embryonic development such hydrocephalus or spina bifida; late pregnancy or perinatal conditions such as retinopathy of prematurity; acquired childhood conditions such bacterial meningitis, measles encephalopathy, near drowning or traumatic brain injury), and conditions of unknown aetiology such as cerebral palsy or autism^{7;14}.

1.1.3.2 Injury related disability

1.1.3.2.1 Traumatic spinal cord injury

Traumatic spinal cord injury (SCI) is a lifelong disabling condition affecting over 40,000 people in the UK. It is estimated that traumatic spinal cord injury affects 10 to 15 people per million population per year. The majority of spinal cord injuries occur in young men, however, the age of onset increasing. The consequence of the majority of injuries is tetraplegia and primarily incomplete injuries¹⁵.

1.1.3.2.2 Traumatic head injury

Approximately 11,000 individuals per year suffer as a severe traumatic brain injury (TBI), defined as Glasgow Coma Score (GCS) score of eight or less. Approximately 50% of those who suffer a TBI will survive¹⁶. Around half of all people admitted to hospital with a head injury will suffer long term physical disability or psychological disturbance as defined by the GCS eight or less¹⁷.

1.1.3.2.3 Dementia

Dementia is a syndrome with a multifactorial aetiology characterised by progressive deterioration in functional ability including memory, higher, reasoning, communication skills and the ability to perform basic activities of daily living. Dementia is also associated with behavioural or psychological symptoms such as agitation, depression, aggression, wandering or psychosis. Approximately 700,000 people in the UK who have dementia. Over the next 30 years the number of people with dementia is expected to double. Dementia is primarily a health condition which affects older people, but there are at least 15,000 people in the UK who are under the age of sixty five and have dementia¹⁸.

1.1.3.2.4 Other health conditions associated with disability

Other health conditions associated with activity limitations such as the ability to brush ones teeth, open medicine bottles or keep safe include: alcohol or drug related problems, acquired immunodeficiency syndrome (AIDS) or AIDs related condition, blindness, cancer, deafness or hearing problem, diabetes, epilepsy, lung or respiratory problems, mental or emotional problems and missing limbs¹⁴.

1.1.4 Long-term care of people with disabling conditions

Management, control and long-term care of people with chronic diseases and disabling conditions presents a major and increasing challenge, for

health care systems around the world. Home-based care is already growing swiftly in all countries. For example, In the United Kingdom, the National Health Service Improvement Plan¹⁹ presented the UK Governments strategy to improve care for people with chronic diseases away from the traditional focus of acute health care, to a patient centred, community care based model. This reorientation of health services away from acute hospital based care is due in part to increasing need but also, in developed countries, for economic reasons.

1.1.5 The need for informal care

Informal care is recognised as an integral and crucial part of health and social care systems²⁰. Informal care is provided by family, friends, and neighbours. The need for informal care is influenced by changing mental, emotional, physiological, or anatomical structures or functions as a consequence of disease, injury, infection, congenital conditions, or other agents. This includes all residual losses or abnormalities, pain and restrictions in function or functional capacity which result from all forms of pathology not just active disease^{7;21}. The need for care is likely to be dynamic and to result from complex interactions among biological, behavioural, psychological, social and environmental factors. The types of activities that people need help with include: assistance with personal care, supervision in the home to prevent accidents, basic health monitoring and medication management on a daily basis.

The scientific and public health motivation for conducting research on informal carers is firstly to determine the health consequences of caring for someone in illness or disability, and to make recommendations for remedial efforts when indicated. Secondly, to reduce the uncertainties that exist about the effects of health and social care interventions that are offered to individual carers or groups of carers, so that better decisions can be made by carers and statutory and non statutory bodies that fund activities and programmes for carers, and to improve health and social care

intervention choices. However, given the immense and invaluable contribution that informal carers make to society, the immediate public, professional and political concern is of course, the protection of the carer.

1.1.6 The historical roots of the word carer

The use of the word carer meaning 'one who cares', dates back at least to the 17th century. However, the word 'carer' meaning 'a person whose occupation is the care of the sick, aged, disabled, etc. also applied to someone who looks after a disabled or elderly relative at home, often at the expense of her or his own career' first entered the Oxford English Dictionary in 1989²². The first evidence for the latter meaning of the word 'carer' comes from an article published in *Age & Ageing* in 1978, entitled 'Why admit stroke patients to hospital?'²³. This study found that the presence or absence of a 'chief carer' influenced who was admitted to hospital. Certain 'chief carer' characteristics were also found to favour admission including 'being male, over 70 and of social classes 3, 4 or 5'. The primary reason for admission given by general practitioners was relatives inability to cope with the stroke patient. However, the Family Carer Alliance²⁴ (now the American Carer Alliance) was established in San Francisco, America in 1977, one year prior to Brocklehursts introduction of the word carer. The aim of the Family Carer Alliance was to address the needs of families and friends who were providing informal care to a loved one who did not 'fit' into the traditional health care system such as those with stroke, Parkinsons disease, traumatic brain injury and other chronic disabling conditions.

Therefore, the use of carer to represent 'one who cares' has been around for several hundred years, however the concept of the 'carer' as a position, or status, within a social environment, that is shaped by certain behavioural expectations is relatively modern phenomenon.

1.1.6.1 The definition of carer

There is no formally agreed definition of informal care or what defines an informal carer, however, several definitions are available. Eurocarers defines a carer 'as a person who provides unpaid care to someone with a chronic illness, disability or other long lasting health or care need, outside a professional or formal framework'²⁵. Carers Scotland defines a carer as someone who provides 'unpaid care by looking after ill, frail or disabled family members, friends or partners'²⁶. The Princess Royal Trust for Carers defines a carer as 'A carer is someone of any age who provides unpaid support to family or friends who could not manage without this help due to illness, disability, mental ill-health or a substance misuse problem'²⁷.

1.1.6.2 Provision of informal care and effect on health

The rapid growth and publication of many studies on the adverse effects of informal care on health related states coupled with the rising tide of social concern for informal carers has led to the development of non-government organizations (NGOs) directed at supporting the advancement and support of carers and policies relating to carers^{25;28}, government strategies²⁰ and government guidance¹⁹ with the aim of providing carers with the best possible health care and support in their role as carers¹⁸⁻²⁰, NGOs such as the Princess Royal Trust for Carers and similar organisations which provide for example help, information, education and training, support and respite care. The surge of research activity has also identified various adverse health endpoints associated with informal care. In one population-based study of the elderly, people who provide care to their spouse and report strain associated with providing care were 63% more likely to die within four years of follow-up than non care giving controls²⁹. In another cohort study of female registered nurses, providing care to a disabled or ill spouse was associated with an almost twofold adjusted risk ratio for experiencing an adverse cardiac event during the four-year follow-up period³⁰. Chronic carer stress has also been associated with both impaired immune and

endocrine function in spousal carers of people with dementia^{31 32}. Other studies have linked care giving to psychiatric morbidity such as depression and anxiety^{33;34}, lower perceived health status³⁵, deficits in immune responses³⁶, altered neuroendocrine status³⁷, elevated blood pressure^{38;39}, gastrointestinal problems⁴⁰, sleep disorders⁴¹, impaired cognitive function⁴², impaired wound healing^{43;44} and fatigue.⁴⁴ The identification of health and disease states as end points of informal care as a causal mechanism has acted as a catalyst and driver for the development and testing of interventions in clinical trials.

Therefore, there are a number of disease outcomes (impaired immune function, depression, anxiety) which are believed to be an effect of providing informal care to people in ill health or disability; that is, disease is the endpoint and providing care is the cause. However, all disease endpoints have a multi factorial aetiology. Further, from correlation alone (such as observed relations between chronic stress in informal carers and immune dysfunction) one cannot infer a causal relation (chronic stress in informal carers causes immune dysfunction). If one action, occurrence or event causes another (press switch & light comes on) then they will be correlated. However, because two things happen together, it does not mean that one caused the other, even if it appears to make sense (providing care causes depression).

Furthermore, the objective of epidemiologic studies of people who provide informal care to is to obtain valid and precise estimates of the effects of the informal care exposure on the occurrence of disease in the source population of a study (internal validity)⁴⁵. Therefore, epidemiological research can be considered *an exercise in measurement*⁴⁵. A further objective can be to obtain estimates which can be generalized to a target population. The bottom line is epidemiologic studies of informal carers are vulnerable to the same types of biases that threaten validity throughout epidemiologic research: confounding, selection bias and information bias⁴⁵.

Aims

This research has four broad research aims. The first aim was to use existing data to determine the relationship between exposure to providing care to another who is sick, elderly or disabled and health related outcomes. The second aim was to provide a thorough summary of the published and unpublished epidemiological literature on the effects of providing care to a stroke survivor on health related outcomes. The third aim was to generate new high quality research on the effects of providing informal care to a stroke survivor on the occurrence of health related outcomes (in a cohort study). The fourth aim was to provide a rigorous summary of the effects of non-pharmacological interventions targeted towards people who are providing informal care to a stroke survivor.

Objectives

1. To evaluate the risk to individuals from exposure to providing informal care to people in ill health or disability, and the possible relationship between amounts of care provided and reported poor health.
2. To evaluate the magnitude and temporal pattern of adverse health risk following exposure to providing informal care to stroke survivors.
3. To obtain valid and precise estimates of the effect of providing informal care on the occurrence of depression in people who provide informal care to stroke survivors.
4. To determine the effects of non pharmacological interventions targeted towards individuals who are involved in providing informal care to stroke survivors.

Chapter 2 Is informal care giving independently associated with poor health? A population-based study

2.1 Introduction to chapter

Causal inferences can be drawn from routinely collected population statistics that include data on provision of unpaid care and poor health. Data from the UK Census 2001 provides a unique opportunity to examine the nature and strength of the relationship between provision (and independent contribution) of informal care and reported poor health whilst simultaneously controlling for a number of important covariates including age, sex, marital status and ethnic group in a data set containing approximately 50 million people.

2.2 Background

Data from the UK Census 2001 estimates that one person in eight (six million people) in the United Kingdom ‘looks after or gives help and support to family members, friends, neighbours or others because of long-term physical or mental ill health or disability, or problems related to old age’⁴⁶. Furthermore, 6.8 million (16% population) people aged 16 and above in the United Kingdom report that they have ‘extra responsibilities because they look after someone who has long-term physical or mental health or disability, or problems related to old age’⁴⁷.

As noted in Chapter 1, providing care to another person has been implicated as a risk factor for poor health⁴⁸. However, population based studies^{29;49;50} and systematic reviews⁵¹ assessing the impact of exposure to informal care giving on health status either focus on a subset of the care giving population (for example women⁴⁹, older people²⁹, spouses living

with care recipient²⁹ or those who require assistance with basic or extended activities of daily living²⁹ and therefore are not generalisable to the informal care giving workforce. Also, many do not take into account factors known to influence health status such as age, gender and socioeconomic status or provide insufficient information to determine whether the carer and comparison groups differ in key characteristics (for example age, gender) which may act as confounders⁵¹.

Aim

The aim of this study was to examine the relationship between self-reported health status and informal care giving to another person because of long-term physical or mental ill health or disability, or problems related to old age.

2.3 Methods

The objectives were to use data from the UK 2001 Census to determine whether the prevalence of reported poor health, a) was higher in those exposed to providing informal care than those who are not exposed to providing care, b) increases as exposure to care giving increases and c) could be explained by the possible confounding effects of age, gender, ethnic group, marital status, economic activity or educational attainment.

Data from the 2001 Census from respondents aged 16 and over were used. This Census was the first to include questions on the provision of unpaid care (Box 2-1, page 2-47) and general health (Box 2-2, page 2-47). For the purpose of this manuscript, participants reporting 'not good' health are referred to as having 'poor health'. The methodology of the 2001 Population Census is described in detail elsewhere⁵². In summary, the Population Census is a survey that collects data from all members of the population living in England, Wales, Scotland and Northern Ireland on Census day and is performed at 10-year intervals. The Census uses self-completion forms.

The survey content includes over 40 questions covering the characteristics of the population such as age, marital status, economic activity, housing and health. A question of care giving was included in the survey from which it is possible to determine whether or not the respondent provided care to another person because of long-term physical or mental ill health or disability, or problems related to old age, and including the number of hours care that they provided on a weekly basis. A question was also included on self-reported health status.

There is no single United Kingdom (UK) Census. The Census for England and Wales is conducted by the Office for National Statistics; the Scottish Census is conducted by the General Register Office for Scotland and the Northern Ireland Census by the Northern Ireland Statistics and Research Agency. The 2001 UK Census response rate for England and Wales is estimated to be 94%⁵³, 96.1% in Scotland⁵⁴ and 95.3% in Northern Ireland⁵⁵.

Data on 46,930,509 (Figure 2-1) respondents aged over 16 were available from the Office for National Statistics (ONS)⁵⁶. In order to remove a potential source of confounding we excluded people who were classified in the economic activity category as 'permanently sick and disabled' (n = 2,464,676, 5.25%) on the basis that many of the subgroup will have had long-standing illness unrelated to care giving status. This left a total of 44,465,833 (94.75%) respondents for inclusion in this analysis.

The outcome of interest was self-reported health status. Analyses adjusted for age, sex, marital status, ethnicity, economic activity and education based on prior knowledge of factors likely to influence health status^{3;57;58}. In addition, the number of variables available for inclusion was limited by the ONS to avoid issues related to confidentiality and disclosure⁵⁹.

Demographic covariates were categorized: age into 10-year group categories; ethnicity (as white, mixed, Asian or Asian British, black or black British and Chinese or other as specified by the ONS⁵⁶ to ensure ethnic

group consistency across the UK (Figure 2-2)); and marital status as in partnership (married, remarried), not in partnership (single, separated, divorced) or widowed.

Economic activity is categorized by the ONS as economically active (full-time, part-time, self-employed, unemployed, full-time students working in the week before Census, or looking for work and available to start within two weeks), economically inactive (retired, full-time student, looking after home/family, aged 75 and over). Education qualifications were categorized as no qualifications or level 1, 2 and 3 by the ONS to ensure consistency across the UK (Figure 2-3), in addition to the categories 'other' and 'aged 75 and over'.

Descriptive statistics were used to examine the characteristics of the sample and prevalence of outcomes and covariates. Differences in proportions were compared using chi-square test. Univariate analyses (unadjusted odds ratios) were used to examine the association between reported health and care giving exposure and with each covariate: age, sex, marital status, ethnic group, economic activity and educational attainment.

As the proportional odds assumption was not fulfilled when the three self-reported health categories were used ('good', 'fairly good', 'not good'), the reported health status responses were dichotomized in to 'good/fairly good' and poor ('not good'). The association between poor health and four levels of care giving exposure: no care, 1-19 hours care per week, 20-49 hours per week and 50+ hours per week was examined; no care was chosen as the reference category. Odds ratios for 'not good' health and their accompanying 95% confidence intervals were computed for each care giving exposure level using binary logistic regression. Additional analyses adjusted for age, sex, marital status, ethnicity, economic activity and educational attainment. Identical categorisation of economic activity and educational attainment for individuals aged 75 and over made simultaneous estimation of their individual regression coefficients inappropriate due to

multicollinearity. Therefore two analyses were performed 1) all ages not adjusting for economic activity and educational qualifications (Model 1), and 2) age groups 16-74 adjusting for all covariates (Model 2). Statistical analyses were performed using Minitab 15 and SAS v9.1.

2.4 Results

The baseline characteristics of all participants are shown in Table 2-1. 40,740,785 (91.6%) of the population reported their general health to be 'good/ fairly good' and 3,725,048 (8.4%) reported their health to be poor. Of those reporting their general health to be 'good/ fairly good', 12.2% report providing care compared to 13.2% of those who report their health to be poor (χ^2 test 3534.43, $p < 0.001$). Therefore the odds of reporting providing informal care in individuals reporting poor health are 10% (95% CI 9.6% to 10.3%; $p < 0.001$) higher than those who report good/fairly good health.

5,451,902 (12.3%) of the participants reported providing care to a family member, friend, neighbour or others because of long-term physical or mental ill health or disability, or problems related to old age. 8.3% of non carers report poor health. For all respondents, the prevalence of 'not good health' was significantly greater in those who reported providing care ($n = 492,747$, 9.0%) compared to those who did not provide care (odds ratio 1.100, 95% CI 1.096- 1.103). Table 2-2 shows the relationship between self-reported health and care giving exposure and all covariates. This table shows that the odds of poor health is increased 1) as level of exposure to care giving increases; 2) with age; 3) for females; 4) for the white ethnic group; 5) for groups classified as economically inactive retired, over 75s and other; and 6) as level of educational attainment decreases.

The full binary logistic regression models are presented in Table 2-3. Model 1, which adds demographic characteristics, reveals a diminished association between care giving and poor health although the association

remains and the strength of association increases as the reported amount of care provided per week increases.

The second model introduces economic activity and educational attainment. The inclusion of these factors does not alter the dose-response relationship between care giving and poor health as seen in Model 1, although it does reduce the strength of the association. We found no important interaction between care giving exposure and each of age, sex, marital status, ethnic group, economic activity and educational attainment.

The model R-Squared values, which indicate the proportion of variance explained, are 15.6% (Model 1) and 13.3% (Model 2).

A sensitivity analysis, including participants classified in the economic activity category as 'permanently sick and disabled' showed very similar results.

2.5 Discussion

The main finding of this study is that people who report providing informal care to 'family members, friends, neighbours or others because of long-term physical or mental ill health or disability, or problems related to old age', have increased odds of reporting poor health compared to those who do not provide informal care. This could not be explained by potential confounders including age, sex, marital status, ethnic group economic and education characteristics. We also found a dose response relationship, with those providing highest number of hours of care reporting the highest rates poor health and those providing the least having the lowest. The magnitude of this association is consistent with the results from other studies that have linked informal care giving with adverse health outcomes^{29;49;50}.

These findings have important societal implications. The health risk associated with providing informal care is relatively modest. However, a large number of people are exposed to this risk; one in 12 people in the UK provides informal care.

This is the largest study addressing the relationship between self-reported care giving exposure and self-assessed general health, using data from all adults living in the UK in 2001 who responded to the population census. In addition, unlike previous studies we have not selected carers of a particular age, sex or care recipient group (for example those suffering from dementia or stroke survivors). Also we have not studied specific health outcomes (for example depression or coronary heart disease) but have focused on a large population using a simple, single item self-rated health status report. Using a one item self-rated health status report is an established and valid method of assessing health status⁶⁰.

There are a number of possible mechanisms for how informal care giving may cause poor health. There are many and varied 'occupational hazards' that care givers may be exposed to. These include physical stress, for example mobilising dependent care recipients. Psychosocial stressors include care giving demands^{29;49;50} and conditions that are at variance with the care-givers needs, existing commitments, expectations or values or exceed their capacity, knowledge or skills; uncertainty; high care giving demands, low control and effort-reward imbalance. Problems with physical conditions can include poor access e.g. stairs, lack of environmental aids and technologies. These same conditions presenting in an employment or work environment would be recognized as physical and psychosocial hazards and therefore risk factors for physical and mental health problems^{58;61}. Although it is yet to be established whether such a model is plausible in explaining the relationship between exposure to informal care provision and stress, elements have been tested in carers of specific groups^{62;63}. In addition, there is an association between stress in informal carers and immune dysregulation⁶⁴, elevated blood pressure⁶⁵, impaired wound healing⁴³ and increased risk of mortality²⁹; there is also increased

risk of coronary heart disease⁴⁹ and poorer cognitive function⁶⁷ among women who provide care to their disabled or ill spouses.

The care giving context including the relationship between the carer and the care recipient may also be important^{49;50}. For example women who provide care to their disabled or ill spouses are more likely to become ill than those who care for other dependent family members⁴⁹.

One limitation of this study is the cross sectional nature. Temporal associations cannot be inferred⁶⁸. It is also difficult to establish whether carers have been exposed to 'care giving' for long enough to develop a change in health status and for the latency period to have elapsed, which is likely to lead to an underestimation of the odds of 'not good' health. In addition, we have compared currently exposed individuals with currently unexposed individuals, this does not account for their recent past history of care giving exposure which may lead to underestimation of the effect of care giving exposure as a risk factor for poor health, or regression dilution bias⁶⁹.

Self-assessed general health status may also affect who takes on the care giving role. For example, in the 65 and over age group it is possible that people who report good or fairly good general health are more likely to take on the care giving role than those reporting not good health, introducing the possibility of membership bias.

The ability to adjust for confounders was limited to those variables available as part of the UK Census 2001 and does not collect for example, information on health behaviours which may influence reported health status⁶⁰. This is reflected by the relatively low R^2 values of the models fitted. In addition, the number of variables available to us was also restricted by measures put in place that uphold the 2001 Census confidentiality commitments⁵⁹. Ideally, we would have included self-reported long-term illness, occupation⁷⁰, national statistics socioeconomic classification (NSEC) and geographical location⁷¹.

The quantification of the time spent in a typical week providing unpaid care including the validity and reliability of the self-reported time estimates must also be taken into consideration along with the potential for reporting inaccuracies among proxy respondents. In addition, the categorization of hours of care giving into 1-19, 20-49 and 50 plus hours care per week prevented a more in-depth analysis of the relationship between care giving and health outcome over the full spectrum of number of hours of care giving. Therefore, there is the possibility of residual confounding as a consequence of measurement imprecision for included covariates, and unmeasured covariates.

However, the cross sectional design is valuable for measuring the population burden of self-reported poor health using prevalence rates. The UK 2001 Census is unique in that it effectively gathers data on people representing almost all stages of health, disease and illness and exposures of interest. In addition, the general health outcome and carer exposure status are clear, specific and measurable. The data have been collected in the same way for the group exposed to care giving and the group not exposed which helps prevent errors in measuring care giving exposure and self-reported health status. Additionally, those who are responsible for processing the results of the UK 2001 Census are blind to the exposure status reducing any risk of detection bias. Also, previous studies have found that a simple, one item self-reported health question similar to that used in this UK 2001 Census was associated with mortality when all other factors known to influence health and prior information about health status were controlled for⁶⁰.

2.6 Conclusions

The results demonstrate that in a cross sectional study of the UK population the prevalence of poor health is greater in those who provide informal care compared to those who do not provide informal care and that this increases with the level of exposure to informal care. In addition, use

of the data from the UK Census 2001 illustrates how a large and valid secondary data source can be accessed within a short period of time to address a research question such as assessing the relationship between exposure to care and reported poor health and to generate further research questions.

2.7 Implications for policy

One of the key challenges facing countries with a burgeoning ageing population and a concomitant rise in prevalence of disability and dependence is meeting the needs of this population without placing excessive demands on informal carers. This dilemma has direct implications for health and social service systems. Currently, the national General Medical Services (GMS) GP contract awards points for establishing of a system to identify carers and liaise with outside agencies; however creation of such a system is voluntary. Formal surveillance systems offer the opportunity to monitor trends in rate of occurrence of ill health. These can be used to anticipate needs, inform plans for health or social care and guide preventative and therapeutic strategies for carers. Moreover, information from surveillance could guide future research priorities. However informal care is a complex and dynamic chronic exposure; use of a clear, unambiguous definition of informal care and an appropriate system for measuring (and reviewing) the informal care exposure is fundamental to the validity of any surveillance system.

2.8 Implications for research

The UK Census 2011 has recently taken place (27TH March 2011). The same data were collected on general health and provision of help and support to family members, friends, neighbours or others because of long-term physical or mental ill-health/ disability or problems related to old age; therefore the UK Census 2011 provides the opportunity to monitor over time, changes in the nature and extent of informal care and associated

health problems. The detection of a change in prevalence of informal care and associated rise in poor health should alert policy makers, health care and social care agencies and the public alike to the need for further investigation.

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‘Do you look after, or give any help or support to family members, friends, neighbours or others because of: long term physical or mental ill health or disability, or problems related to old age?’

Do not count anything you do as part of your paid employment.

√ Time spent in a typical week

- No
- Yes, 1-19 hours per week
- Yes, 20-49 hours per week
- Yes, 50+ hours per week

Box 2-1 Question on care giving activities from the UK Census 2001

Over the last twelve months would you say your health on the whole has been:

- Good?
- Fairly good?
- Not good?

Box 2-2 Question on health from the UK Census 2001

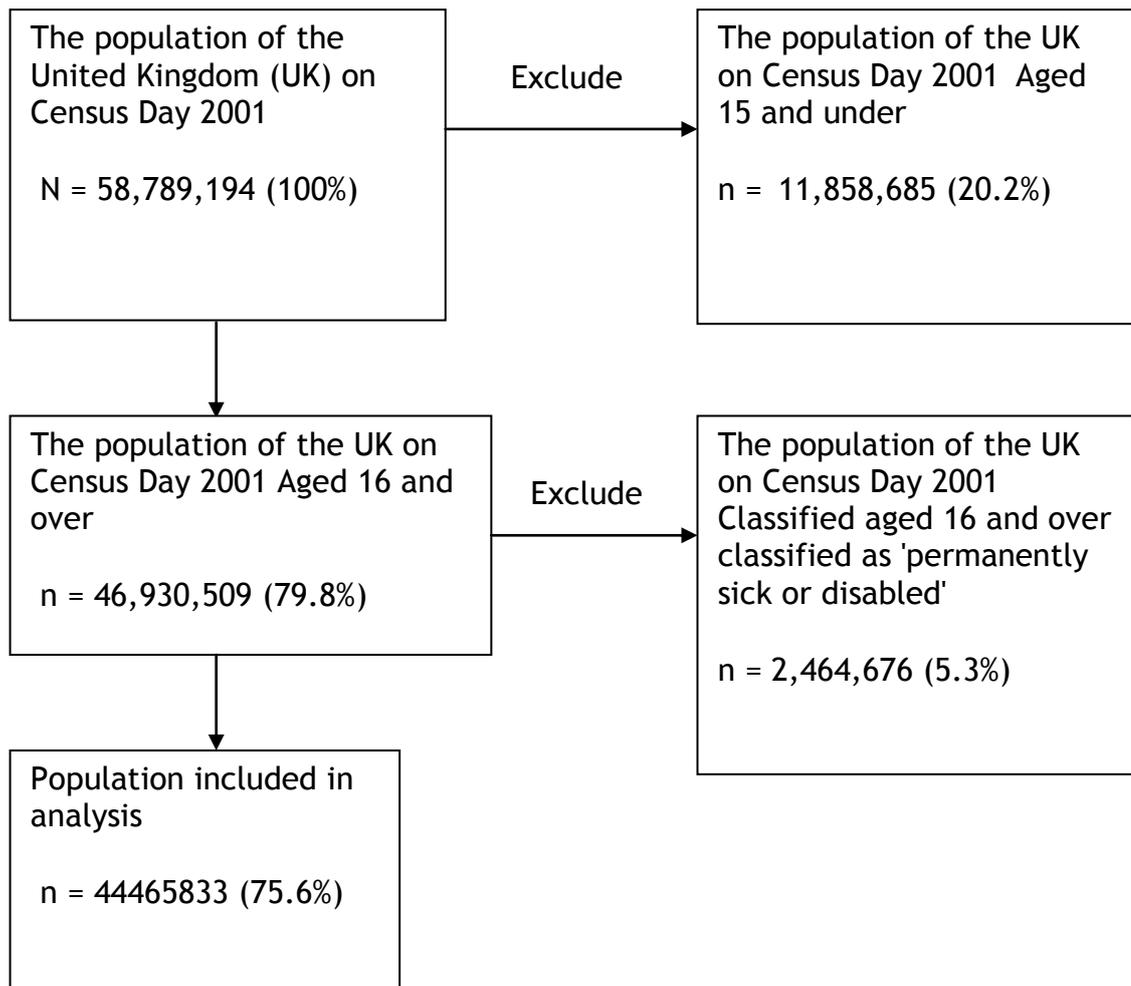


Figure 2-2 Flowchart of subjects included and excluded in analysis of association of informal care giving with self-reported 'not good' health.

Cells in Census tables have been randomly adjusted to avoid the release of confidential data. Totals are created by the summing of adjusted counts and are internally additive within a table in order to protect the confidentiality of the individual. Consequently the counts in this flowchart may differ slightly from those in other published table.

UK Ethnic group codes	Ethnic group in England and Wales	Ethnic group in Northern Ireland	Ethnic group in Scotland
White	British, Irish, other white	White, Irish Traveller	White Scottish, other white British, white Irish, other white
Mixed	White and Black Caribbean, White and Black African, White and Asian, Other mixed	Mixed	Any mixed background
Asian or Asian British	Indian, Pakistani, Bangladeshi, other Asian	Indian, Pakistani, Bangladeshi, other Asian	Indian, Pakistani, Bangladeshi, other South Asian
Black or black British	Black Caribbean, Black African, other Black	Black Caribbean, Black African, other Black	Caribbean, African, Black Scottish or other Black
Chinese or other	Chinese, other ethnic group	Chinese, other ethnic group	Chinese, other ethnic group
UK Ethnic group codes	Ethnic group in England and Wales	Ethnic group in Northern Ireland	Ethnic group in Scotland

Figure 2.2 United Kingdom ethnic group codes for each of the ethnic group variables for each UK country: England and Wales, Northern Ireland and Scotland.

UK Level of Qualifications codes	England and Wales	Northern Ireland	Scotland
No qualifications	No academic or professional qualifications	No Qualifications	No Qualifications
First	1+ O levels/CSE/GCSE (any grades), NVQ, Foundation GNVQ, 5+ O levels, 5+CSEs (grade 1), 5+GCSEs (grades AC) etc, 1+ A levels/AS levels, NVQ level 2, Intermediate GNVQ	GCSEs (grades DG), CSEs (grades 25), 14 CSEs (grade 1), 14 GCSEs (grades AC) etc, NVQ level 1, GNVQ foundation 5+ CSEs (grade 1) 5+ GCSEs (grades AC) etc, 1 'A' level, 13 AS level etc, NVQ level 2, GNVQ Intermediate	O' Grade, Standard Grade, GCSE, CSE etc, GSVQ/SVQ Level 1 or 2, SCOTVEC module etc
Second	2+ A levels, 4+ AS Levels, Higher School Certificate, NVQ level 3, Advanced GNVQ	2+ 'A' levels, 4+ AS levels, NVQ level 3, GNVQ Advanced	Higher Grade, CSYS, 'A' level etc, GSVQ/SVQ Level 3, ONC, OND etc (Scotland)
Third	First degree, Higher degree, NVQ levels 45, HNC, HND Prof qual: Qualified Teacher Status, Qualified Medical Doctor, Qualified Dentist, Qualified Nurse	First degree, NVQ level 4, Higher degree, NVQ level 5	HNC, HND, SVQ level 4 or 5 etc, First degree, higher degree, Professional Qualifications

Figure 2-3 United Kingdom highest qualifications group codes for each level of academic achievement for each UK country: England and Wales, Northern Ireland and Scotland

Table 2-1 Baseline characteristics of all participants by care giving exposure level (n =44465833).

Based on responses to the general health question in the 2001 Census of UK population.

	Not a carer	Yes 1-19 hours care a week	Yes 20-49 hours care a week	Yes 50+ hours of care per week
	N (%)	N (%)	N (%)	N (%)
Sex				
Male	18,907,071(89.31)	1,596,266(7.54)	237,731(1.12)	429,024(2.03)
Female	20,106,860(86.31)	2,132,753 (9.16)	368,291(1.58)	687,837(2.95)
Age				
16-24	6,084,129(95.34)	230,674(3.62)	36,174(0.57)	30,459(0.48)
25-34	7,535,009(92.75)	406,023(5.00)	70,976(0.87)	111,853(1.38)
35-44	7,327,881(87.57)	728,314(8.70)	120,966(1.45)	190,895(2.28)
45-54	5,708,598(80.13)	1,062,437(14.91)	146,362(2.05)	207,038(2.91)
55-64	4,289,886(79.59)	768,111(14.25)	122,110(2.27)	209,880(3.89)
65-74	4,013,344(85.88)	380,117(8.13)	69,618(1.49)	210,152(4.50)
75-84	2,975,683(90.70)	136,549(4.16)	34,556(1.05)	133,887(4.08)
85 and over	1,079,401(96.03)	16,704 (1.49)	5,260(0.47)	22,697(2.02)
Ethnic group				
White	36,255,690(87.62)	3,521,999(8.51)	549,371(1.33)	104,905(2.54)
Asian or Asian British	1,370,344(87.03)	122,962(7.81)	36,647(2.33)	44,563(2.83)
Black or Black British	739,651(91.14)	47,548(5.86)	11,684(1.44)	12,677(1.56)
Chinese or other ethnic group	353,403(93.18)	16,286(4.29)	4,316(1.14)	5,251(1.38)
Mixed	294,843(90.89)	20,224(6.23)	4,004(1.23)	5,318(1.64)
Marital Status				
Partnership	18,962,366(83.61)	2,481,036(10.94)	399,712(1.76)	837,309(3.69)
Alone	16,478,251(91.60)	1,089,113(6.05)	184,477(1.03)	237,860(1.32)
Widowed	3,573,314(94.14)	158,870(4.19)	21,833(0.58)	41,692(1.10)
Economic activity				

	Not a carer	Yes 1-19 hours care a week	Yes 20-49 hours care a week	Yes 50+ hours of care per week
	N (%)	N (%)	N (%)	N (%)
Economically active				
Full-time	15,406,634(89.58)	1,451,515(8.44)	170,892(0.99)	168,866(0.98)
Part-time	4,155,506(83.72)	616,325(12.42)	87,511(1.76)	104,465(2.10)
Self-employed	3,002,809(86.81)	369,926(10.70)	38,898(1.12)	47,229(1.37)
Unemployed	1,303,511(89.37)	108,143(7.41)	22,536(1.55)	24,360(1.67)
Full-time student	1,048,154(94.73)	48,888(4.42)	5,781(0.52)	3,640(0.33)
Economically inactive				
Retired	4,821,374(83.59)	570,215 (9.89)	100,611(1.74)	275,379(4.77)
Full-time student	1,903,442(95.45)	72,671(3.64)	9,571(0.48)	8,494(0.43)
Looking after home/family	2,082,178(75.91)	263,581(9.61)	107,871(3.93)	289,289(10.55)
Other				
Age 75 and over	4,055,084(92.06)	153,253(3.48)	39,816(0.90)	156,584(3.55)
Other	1,235,239(90.11)	74,502(5.43)	22,535(1.64)	38,555(2.81)
Educational attainment				
No qualifications	9,590,994(86.11)	846,660(7.60)	225,790(2.03)	474,394(4.26)
First level	12,611,869(87.86)	1,300,863(9.06)	180,741(1.26)	260,464(1.81)
Second level	3,357,311(90.20)	287,964(7.74)	34,153(0.92)	42,704(1.15)
Third level	7,387,676(87.73)	843,957(10.02)	79,387(0.94)	109,993(1.31)
Other	2,010,997(82.89)	296,322(12.21)	46,135(1.90)	72,722(3.00)

Table 2-2 Relation between reported general health status and covariates.

The full binary logistic regression models are presented in Table 3. Model 1, which adds demographic characteristics, reveals a diminished association between care giving and poor health.

	Good/Fairly good health N = 40740785	Not good health N = 3725048	Crude odds ratio (95% CI)	Univariate analysis
Exposure levels				
No care*	35,781,630(91.7)	3,232,301(8.28)	1	χ^2 test 97214.651, DF = 3, P <0.001
1-19 hours per week	3,477,365(93.3)	251,654(6.75)	0.801(0.796-0.804)	
20-49 hours per week	541,086(90.0)	64,936(10.72)	1.329(1.312-1.348)	
50+ hours per week	940,704(84.2)	176,157(15.77)	2.073(2.055-2.085)	
Sex				
Male*	19,653,196(92.8)	1,516,896(7.17)	1	χ^2 test 77339.977, DF= 1, P <0.001
Female	21,087,589(90.5)	2,208,152(9.48)	1.357 (1.354-1.360)	
Age				
16-24*	6,252,826(98.0)	128,700(2.0)	1	χ^2 test 3737382.723, DF = 7, P <0.001
25-34	7,878,875(97.0)	244,986(3.0)	1.511(1.493-1.527)	
35-44	8,006,582(95.7)	361,474(4.3)	2.193(2.174-2.217)	
45-54	6,684,634(93.8)	439,801(6.2)	3.197(3.174-3.226)	
55-64	4,884,157(90.6)	505,830(9.4)	5.032(4.994-5.066)	
65-74	389,3234(83.3)	779,997(16.7)	9.734(9.674-9.796)	
75-84	2,407,804(73.4)	872,871(26.2)	17.613(17.604-7.726)	
85 and over	732,673(65.2)	391,389(34.8)	25.954 (25.943-26.137)	
Ethnic group				
White*	37,869,450(91.5)	3,506,662(8.5)	1	χ^2 test 12209.963, DF = 4, P <0.001
Asian or Asian British	1,453,435(92.3)	12,1081(7.7)	0.900(0.884-0.916)	
Black or black British	751,181(92.6)	60,379(7.4)	0.868(0.852-0.885)	
Chinese/other	362,667(95.6)	16,589(4.4)	0.494(0.474-0.516)	
Mixed	304,052(93.7)	20,337(6.3)	0.722(0.696-0.745)	
Marital status				
Married*	18,072,531(92.2)	1,520,888(7.8)	1	χ^2 test
Single	13,004,841(95.9)	552,643(4.1)	0.505(0.497-0.513)	

	Good/Fairly good health N = 40740785	Not good health N = 3725048	Crude odds ratio (95% CI)	Univariate analysis
Re-married	2,803,170(90.8)	283,834(9.2)	1.203(1.196-1.214)	1625415.315,DF = 5, P <0.001
Separated	978,315(90.9)	98,326(9.1)	1.194(1.183-1.207)	
Divorced	3,012,639(89.8)	342,937(24.4)	1.353(1.346-1.364)	
Widowed	2,869,289(75.6)	926,420(24.9)	3.837(3.827-3.853)	
Economic activity				
Economically active				
Full-time*	16,688,517(97.0)	509,390(3.00)	1	χ^2 test 4140446.991, DF = 9, P <0.001
Part-time	4,760,935(95.9)	202,872(4.1)	1.396(1.385-1.405)	
Self-employed	3,326,278(96.2)	132,584(3.8)	1.306(1.294-1.316)	
Unemployed	1,353,242(92.8)	105,308(7.2)	2.549(2.523-2.577)	
Full-time student	1,089,245(98.4)	17,218(1.6)	0.518(0.494-0.546)	
Economically inactive				
Retired	481,0854(83.4)	956,725(16.6)	6.515(6.464-6.544)	
Full-time student	1,943,301(97.5)	50,877(2.6)	0.858(0.841-0.879)	
Looking after home/family	2,529,188(92.2)	213,731(7.8)	2.769(2.745-2.785)	
Other				
Aged 75 and over	3,140,477(71.3)	1,264,260(28.7)	13.189(13.137-3.234)	
Other	1,098,748(80.2)	272,083(19.9)	8.113(8.065-8.155)	
Educational attainment				
Third level*	8,104,305(96.2)	316,708(3.8)	1	χ^2 test 3203627.813, DF = 5,P <0.001
No qualifications	9,881,279(88.7)	1,256,559(11.3)	3.254(3.236-3.274)	
First level	13,776,693(96.00)	577,244(4.0)	1.072(1.065-1.085)	
Second level	3,595,330(96.6)	126,802(3.4)	0.902(0.893-0.917)	
Other	2,242,701(92.4)	183,475(7.6)	2.093(2.074-2.116)	
Aged 75 and over	3,140,477(71.3)	1,264,260(28.7)	10.301(10.26-10.34)	

Table 2-3 Full binary logistic regression models. Model 1: all ages not adjusting for economic activity and educational qualifications and model 2, age groups 16-74 adjusting for all covariates.

Odds ratios are for 'not good' health.

	N (%)	Model 1: All Odds ratio (95% CI)	Model 2: 16-74 Odds ratio (95% CI)
Exposure levels			
No care	39,013,931(87.74)	1	1
1-19 hours per week	3,729,019(8.39)	0.877(0.873-0.881)	1.019(1.005-1.025)
20-49 hours per week	60,602(1.36)	1.355(1.344-1.367)	1.281(1.261-1.299)
50+ hours per week	111,686(2.51)	1.670(1.661-1.680)	1.461(1.443-1.477)
Sex			
Male	21,170,092(47.61)	1	1
Female	23,295,741(52.39)	1.138(1.138-1.142)	0.988(0.977-0.993)
Age			
16-24	6,381,526(14.35)	1	1
25-34	8,123,861(18.27)	1.691(1.673-1.707)	1.823(1.802-1.848)
35-44	8,368,056(18.82)	2.675(2.653-2.697)	2.853(2.822-2.878)
45-54	7,124,435(16.02)	4.084(4.053-4.117)	4.070(4.032-4.108)
55-64	5,389,987(12.12)	6.505(6.453-6.557)	4.269(4.232-4.308)
65-74	4,673,231(10.51)	12.353(12.263-12.437)	4.937(4.881-4.989)
75 - 84	3,280,675(7.38)	21.437(21.293-21.587)	
85 and over	1,124,062(2.53)	29.877(29.642-30.108)	
Ethnicity			
White	41,376,112(93.05)	1	1
Mixed	324,389(0.73)	1.398(1.365-1.435)	1.342(1.304-1.376)
Asian or Asian British	1,574,516(3.54)	1.703(1.684-1.716)	1.388(1.373-1.407)
Black or black British	811,560(1.83)	1.364(1.341-1.389)	1.232(1.210-1.250)
Chinese or group	379256(0.85)	0.943(0.914-0.976)	0.837(0.803-0.867)
Marital status			
In partnership	22,680,423(51.01)	1	1

	N (%)	Model 1: All Odds ratio (95% CI)	Model 2: 16-74 Odds ratio (95% CI)
Not in partnership	17,989,701(40.46)	1.402(1.397-1.413)	1.434(1.427-1.443)
Widowed	3,795,709(8.54)	1.254(1.247-1.263)	1.161(1.155-1.175)
Economic activity			
Economically active			
Employee Full-time	17,197,907(38.68)		1
Employee Part-time	4,963,807(11.16)		1.230(1.214-1.246)
Self-employed	3,458,862(7.78)		1.069(1.054-1.086)
Unemployed	1,458,550(3.28)		2.396(2.373-2.417)
Full time students	1,106,463(2.49)		0.993(0.964-1.026)
Economically inactive			
Retired	5,767,579(12.97)		3.349(3.324-3.376)
Full-time student	1994178(4.49)		1.596(1.569-1.621)
Looking after home/family	2742919(6.17)		2.354(2.334-2.376)
Other			
Aged 75 and over	4,404,737(9.91)		
Other	1,370,831(3.08)		6.265(6.225-6.305)
Educational attainment			
Third level	8,421,013(18.94)		1
No qualifications	11,137,838(25.05)		1.749(1.736-1.764)
First level	14,353,937(32.28)		1.207(1.195-1.215)
Second level	3,722,132(8.37)		1.199(1.183-1.217)
Other Qualifications	2,426,176(5.46)		1.482(1.464-1.496)
Aged 75 and over	4,404,737(9.91)		

Chapter 3 The Glasgow Carers Cohort Study: informal care giving and risk of disease

3.1 Introduction to chapter

The analysis of the UK Census 2001 data set (Chapter 2) found a strong association and an exposure-response relationship between provision of informal care and reported poor health with the likelihood of reporting poor health increasing as the number of hours care provided per week increased. However, strength of association is not sufficient to determine that provision of informal care to someone who is in ill health or disability is a cause of poor health. The observed association may be partly or totally due to unknown or unmeasured confounders. Equally, the presence of a steadily increasing exposure-response curve does not provide sufficient evidence of a causal relationship because of unknown or unmeasured confounders that may be in operation. The sine qua non for evidence of a causal relationship is that the cause, in this case exposure to providing informal care, must precede the effect, in this instance reported poor health. Given that the UK Census 2001 is a cross sectional study, it was not possible to determine the temporal nature of the relationship between provision of informal care and poor health. In response to this, the Glasgow Carers Cohort Study (GCCS), a matched cohort study, was established. The specific focus of GCCS is people who look after or provide help and support to stroke survivors who live at home after discharge from hospital following acute stroke onset.

3.2 Background

3.2.1 Defining Stroke

The World Health Organization defines stroke as ‘a syndrome of rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than vascular origin’⁷². Stroke is an umbrella term for a range of subtypes with different risk factors and outcomes. The two main pathological classifications are ischaemic and haemorrhagic stroke⁷³.

3.2.1.1 Ischaemic stroke

Ischaemic stroke occurs when the main arteries supplying the brain with fresh blood from the heart and lungs become narrowed or hardened (atherosclerosis or atheroma), or obstructed. Ischaemia can be further broken down into aetiologic subtypes and clinical presentations. Aetiologic subtypes⁷⁴ include:

- large-artery atherosclerosis, characterised by significant narrowing or constriction (stenosis) or blockage (occlusion) of a major brain artery or a branch cortical artery, as a likely consequence of atherosclerosis;
- cardioembolism, characterised by arterial occlusions as a likely consequence of a piece of a blood clot (embolus) coming from the heart;
- small artery occlusion (lacunar infarcts⁷⁵) characterised by occlusion of a single perforating artery of the brain;
- stroke of other determined aetiology including; 1) nonatherosclerotic vascular disease including a. non-inflammatory vascular diseases (for example arterial dissection, arterial trauma, fibromuscular dysplasia etc)), b. infection (for example syphilis, acquired immune deficiency syndrome, bacterial meningitis etc), c. inflammatory non-infectious vascular diseases (for example multi-system vasculitis, isolated central nervous system vasculitis). 2) Hypercoagulable states and haematological disorders (for example Sickle Cell disease, thrombocytosis polycythemia, thrombocytopenia, leukaemia) or hypercoagulable states secondary to other conditions (for example pregnancy and puerperium, inflammatory bowel disease, cancer and chemotherapy).
- undetermined aetiology⁷⁴.

3.2.1.2 Haemorrhagic stroke

Haemorrhagic stroke can be broken down into intracerebral haemorrhage and subarachnoid haemorrhage. Intracerebral haemorrhage is focal bleeding from a small artery in a part of the brain which is essential to its functioning (parenchyma). Intracerebral haemorrhage usually occurs as a consequence of a ruptured arteriosclerotic small artery that has been weakened, usually by chronic arterial hypertension⁷⁶.

Subarachnoid haemorrhage is a spontaneous bleeding into the subarachnoid space, between the arachnoid and pia mater. The most common cause of sudden bleeding is a ruptured small saccular aneurysm (berry aneurysm) of a cerebral artery, usually at the junction of the circle of Willis.

3.2.2 The consequences of stroke

The neurological symptoms that a patient presents with will depend on which cerebral artery has been affected. Clinical presentations of cerebral infarction include total anterior circulation syndrome (TACS), partial anterior circulation syndrome (PACS), posterior circulation syndrome (POCS) and lacunar infarcts (LACS)⁷³.

3.2.2.1 Total anterior circulation syndromes (TACS)

The clinical features of TACS are hemiplegia usually with ipsilateral motor and/or sensory deficit of at least two areas of the face, arm and leg; new higher cortical deficits (dysphasia, dyscalculia, apraxia, hemineglect, visuospatial deficits); and homonymous visual field deficit (a loss of vision on the same side in both eyes)^{73;77}. This is the most severe form of stroke in the classification system.

3.2.2.2 Partial anterior circulation syndromes (PACS)

Symptoms of partial occlusion of the anterior circulation supplying one side of the brain are known as a partial anterior circulation syndrome (PACS). The clinical features of PACS are motor/ sensory deficit & hemianopia; motor/ sensory deficit and new higher cerebral dysfunction; newer higher cerebral dysfunction and hemianopia; pure motor/ sensory deficit less extensive than for lacunar syndromes; or new higher cerebral dysfunction alone (for example aphasia)⁷⁷.

3.2.2.3 Posterior circulation syndromes (POCS)

Posterior cerebral artery stroke is less common than an anterior circulation artery stroke. Clinical features of infarcts in the posterior circulation are cranial

nerve palsies, gaze palsies, bilateral motor or sensory deficit, ataxia, isolated hemianopia or cortical blindness, and vertigo⁷⁷.

3.2.2.4 Lacunar syndromes (LACS)

Lacunar syndrome (LACS) are usually caused by small deep infarcts that usually occur in the territory of a single deep penetrating artery. Lacunar infarcts occur in the lenticular nucleus, the putamen, thalamus and white matter of the internal capsule, pons and centrum semiovale⁷⁵. There are four categories of LACS: pure motor stroke (PMS) (hemiparesis affecting the face, arm, and leg on the same side sparing sensation, vision, language and behaviour⁷⁸); pure sensory stroke (PSS)(affects sensation over the entire side of the body, involving the face, proximal and distal limbs and axial structures including the scalp, neck, trunk and genitalia⁷⁸); ataxic hemiparesis (including dysarthria, clumsy hand syndrome and homolateral ataxia and crural paresis) (AH); or sensori-motor stroke (SMS).

In summary, stroke is a complex disease with many forms and diverse pervasive sequelae which can affect the functioning of specific body systems, generic physical and mental actions and in turn the ability to perform activities of daily living.

3.2.3 *Living with stroke*

Stroke can affect a persons ability to perform activities in any domain of life. Activity domains include basic personal care (feeding, dressing, toileting, bathing, mobility indoors, transferring on and off bed, toilet or chair); extended activities of daily living (including preparing food, light housekeeping, manage own money, shopping for personal items, laundry, recreational activities, socialising with friends); communication; paid employment; caring for children and others; and participation in and commitment to prescribed medical care (i.e., drug interventions etc.), rehabilitation and health promotion activities. Therefore the needs of the stroke survivor can be complex, numerous and chronic. In addition stroke survivors may need psychological and emotional support (including learning to cope with life after stroke); and help to resume as normal a life as possible^{79;80}. Based on UK estimates of population aged 15 and

above (50,647,500)^{81;82} at any one time, approximately 232,980 (0.46%)⁸³ people will be limited in their ability to perform activities of daily living and 86,100 (0.17%)⁸³ will require assistance with self-care as a consequence of stroke.

3.2.4 The need for informal care

The gaps that exist between the activities the stroke survivor needs to perform and their actual abilities in any activity domain are often met by assistance from another person i.e., a family member or friend. Family and friends who fill the gaps by providing care and support to stroke survivors are often referred to as informal or unpaid carers. These informal carers are recognized to be a vital resource for stroke survivors⁸⁴⁻⁸⁶. Informal carers strive to meet the needs of the stroke survivor while simultaneously adjusting emotionally and practically to an often new and different life with the stroke survivor. However, while being an informal carer can be a rewarding experience⁸⁷ for many the demands placed on them can be relentless and unlimited.⁷⁹

As stroke is estimated to be the commonest cause of complex disability, it provides a unique opportunity to study the effects of providing care on the care provider.

The idea that providing informal care to stroke survivors is a risk factor in the development of poor health is widespread in the general population and among health professionals. The prevailing hypothesis for such an association is that the physical and psychosocial demands and obligations of the care giving situation are at variance with the values, attitudes, expectations⁸⁸, desires⁸⁹, knowledge, skills, abilities^{90;91}, and existing commitments⁹⁰ of the carer, physical and mental energy available to the carer⁸⁹, coupled with the effort-reward imbalance⁹² can lead to stress which can in turn predispose the carer to the initiation or progression of ill health which will subsequently affect the carers physical and psychological well being and role performance and productivity.

There are many potential endpoints of interest in an epidemiologic study of informal care exposure. A review of the literature on a wide range of informal carers (See chapter 1) and informal discussions with health care professionals and lay people suggested that psychological and physiological stress, depression

and psychosomatic symptoms were the main components of health related states that were most likely to be affected by informal care giving.

Cohort study hypothesis

A cohort study design can provide comprehensive information on the health effects of the informal care exposure.

1. Providing informal care to stroke survivors precedes 'adverse health outcomes.'
2. The risk of 'adverse health outcomes' will be higher than expected in a population providing informal care to stroke survivors.

The primary adverse health outcome of interest is perceived stress.

Aims

1. To investigate the temporal relationship between providing informal care to stroke survivors and adverse health outcomes.
2. To determine whether the incidence of reported adverse health outcomes is higher in those exposed to providing informal care to stroke survivors than those who are not exposed to providing informal care.
3. To examine whether any excess risk, if found, could be explained by the possible confounding effects of age, gender, ethnic group, marital status, economic activity, educational attainment, history of depression, the presence of co-morbid conditions, lifestyle and behaviour or other factors.

3.3 Methods

3.3.1 Study design

This is a prospective, matched, cohort study recruiting two groups of people that differ with regards to their level of exposure to providing informal care. The exposed cohort is a group of people exposed to providing informal care to a

stroke survivor, the putative causal condition. The other group is the unexposed or reference cohort, that is they are not exposed to providing informal care to anyone in illness, frailty or disability.

3.3.1.1 Definition of cohorts and study groups

For the purpose of this research exposure groups are defined at the start of follow-up, with no consideration of movement of individuals between exposure groups during the follow-up.

3.3.2 Study setting

This study was based in three hospital stroke units in Glasgow, Scotland, UK. All participants were recruited between 30th October 2008 and 16th February 2010.

3.3.3 Sampling planning

It was estimated that a sample size of 103 in each group will have 80% power to detect a difference in means of 2.5 assuming that the common standard deviation is 6.35 using a two-sample t-test with a 5% two sided significance level. The difference in means was based on Perceived Stress Scale (PSS-10) (the primary outcome) normative data from a large national probability sample⁹³. The actual value of 2.5 was derived from the socio demographic categories; 1) Number of people in household (greater than four children in a household versus no children in a household) and 2) Number of children in household (greater than five people in a household versus one person in a household). These two demographic categories were thought to be closest to the stressful demands subject providing practical support to a stroke survivor would be likely to face. To account for anticipated drop out of 10%, 115 exposed and 115 unexposed participants were the target numbers for each exposed and unexposed group.

3.3.4 Participants

3.3.4.1 Inclusion criteria

Participants in both exposed and non exposed cohorts had to be at least 16 years of age, free from any informal care-giving activities in excess of 20 hours per week for example to an elderly dependent relative or a disabled child, able to speak English and mentally capable of participating in a longitudinal study at their cohort entry date.

3.3.4.2 Exclusion criteria

Participants in both the exposed and non exposed cohorts were excluded if they indicated that the presence of one or more clinical conditions from the Charlson comorbidity index⁹⁴ which would suggest serious ill health.

3.3.4.3 Identification and recruitment of the potentially exposed cohort

Eligible participants were all people who identified themselves as likely to be the main provider of care to patients with a clinical diagnosis of stroke who had been admitted to one of the three hospital stroke units and have a post hospital discharge destination of a private address. Engagement in what is necessary for the health, welfare, maintenance and protection of the stroke survivor/ care recipient was confirmed at three and six months after the stroke patient was discharged from hospital by questionnaire. The questionnaire included a series of questions covering the types of activities of daily living that the subject may provide regular help with and, the estimated number of hours care per week that they give help or support to the person that they care for.

After referral or identification following routine screening of a possible stroke patient, the attending clinician or the stroke specialist nurse was contacted to confirm the clinical diagnosis. Stroke patients were excluded if they had a terminal illness (e.g., cancer, heart disease, chronic obstructive pulmonary disease) with a predicted survival of less than six months as estimated by their physician, had a diagnosis of subarachnoid haemorrhage or were resident in a long-term care facility, residential facility or nursing home prior to admission to

a stroke unit, or were being discharged to a long-term care facility, residential facility or nursing home.

Eligible stroke patients were monitored routinely during hospital visiting hours to identify family, friends or neighbours who may engage in the provision of help and support to the stroke patient after discharge from hospital. Medical, nursing and therapy staff also notified the researchers of potentially eligible family, friends or neighbours.

A consecutive sample of potentially eligible participants was provided with written information (see appendix 1) about the GCCS and the opportunity to discuss the study with the principal investigator should they wish. Once the potential participant had consented (see appendix 2) to participate they were asked to complete the eligibility screening questionnaire (see appendix 3). The eligibility screening questionnaire included questions on: 1) whether the person completing the form is likely to be the main person providing the help or support to the stroke survivor; 2) the extent of existing care giving commitments to family members, friends, neighbours or others because of long-term physical or mental ill health or disability, or problems related to old age; and 3) the presence of clinical conditions included in the Charlson Index⁹⁴. Potentially exposed participants who met the inclusion criteria were then asked to complete the baseline questionnaire (see appendix 4). The method of returning all the forms was agreed at each stage with the potential participant. Methods of return included in person to the principal investigator or a member of staff from the Scotland Stroke Research Network (SSRN)⁹⁵; by post using the stamped addressed envelope provided; or to leave it in the in-tray in the stroke unit clearly marked 'for the attention of the principal investigator GCCS' or 'for the attention of SSRN staff member'.

The nature of the recruitment process i.e., consent before screening for eligibility was found to be upsetting for some potential recruits as many who were keen to participate discovered following screening that they were ineligible because of their existing care-giving commitments. Therefore, if it were possible, the researchers identified people who were likely to be at risk of exclusion following screening either through discussions with medical, nursing or therapy staff or an informal discussion with the potential participants. These

potential participants were provided with the same written information but the inclusion and exclusion criteria were highlighted to them.

3.3.4.4 Identification and recruitment of reference group

Age sex matched unexposed subjects were recruited from a general practitioners list of patients, through the Scottish Primary Care Research Network (SPCRN)⁹⁶ funded by the Chief Scientist Office (CSO) and run by the Scottish School of Primary Care, University of Glasgow. Potential age sex matched unexposed subjects were identified by the SPCRN's research officer from the general practitioner's information technology system (GPASS) using a programme written in Excel. In the first instance, for every one person identified as providing practical support to a stroke survivor, ten potential age sex matched subjects were identified and written to. When that recruitment strategy failed to attract sufficient numbers, the ratio of potential age sex matched pair members was increased to one to twenty.

All potential age sex matched pair members were contacted initially by letter from a general practitioner (See appendix 5). This letter informed the potential matched pair member about the study and asked them to return an 'expression of interest' form (see appendix 6) in the stamped addressed envelope (SAE) provided directly to the principal investigator, indicating if they were interested or would like more information before deciding to proceed. Every potential matched pair member who responded was sent a letter (see appendix 7), full study information (see appendix 8), a consent form (see appendix 9) and an SAE. They were also provided with my contact details including telephone number and email address, should they wish to discuss the study or any concerns they may have. When potential matched pair members did call for further information or to discuss concerns, their telephone number was noted and they were called back immediately. Once potential matched pair members had consented to participate, a screening form (see appendix 10) was sent out with an SAE. When participants failed to meet the inclusion criteria, they were contacted by telephone and the reason for exclusion was explained. Potential matched pair members who met the inclusion criteria were sent a letter, the baseline questionnaire and an SAE (see appendix 11).

Each matched pair member was recruited and consented within one year of the exposed participant providing practical care.

It was possible for a non-exposed participant to become exposed during follow-up.

For details of the results of recruitment based on matching see Table 3-2 Matching characteristics, page 3-83.

3.3.4.5 The Scotland Stroke Research Network and recruitment

The study was formally adopted by the Scotland Stroke Research Network (SSRN), whose objectives include helping,

“...expedite the efficient and timely coordination of high quality clinical studies, including their approval, start-up and also recruitment to target and timescale.”⁹⁷

Adoption by the SSRN therefore provided more resources for recruitment.

3.3.5 Follow-up

Follow-up was at three and six months after enrolment. A postal questionnaire was sent out to exposed participants and non exposed participants at each time point.

3.3.6 Data collected

3.3.6.1 Socio-demographic, lifestyle, psychosocial and health data

Socio-demographics measured include: marital status, education, ethnic group and economic activity. *Employment status* was assessed using a validated questionnaire⁵² and categorised in to economically active and economically inactive. *Deprivation score* was based on post code and determined using the Scottish Index of Multiple Deprivation (SMID) deprivation data zones which are categorized into deciles. Deciles are ranked in order of level of deprivation, one being the least deprived and 10 the most deprived⁹⁸. *Educational attainment* was measured using a validated questionnaire⁵² and categorized into four levels:

Level 1: no qualifications; Level 2: O' Grade, Standard Grade, GCSE, CSE etc, GSVQ/SVQ Level 1 or 2, SCOTVEC module etc; Level 3: Higher Grade, CSYS, 'A' level etc, GSVQ/SVQ Level 3, ONC, OND etc (Scotland)⁵²; or Level 4: HNC, HND, SVQ level 4 or 5 etc, first degree, higher degree, Professional Qualifications. Data on financial worries were also collected using a simple question, 'Are you worried about any financial debt that you might be in?' Responses to this question were 'Yes' or 'No'.

Health behaviours measured were cigarette consumption and alcohol consumption using questions derived from a validated questionnaire⁹⁹. Alcohol consumption was summarized as frequency of consumption: none, monthly or less, two to four times per week and four or more times per week and amount of alcohol consumed on a daily basis when drinking. Cigarette consumption was categorized as never-smokers, former smokers, current smokers and daily cigarette consumption.

Health data measured were health related quality of life using the RAND 36-Item Health Survey 1.0¹⁰⁰, the presence of comorbid clinical conditions as measured by the The Charlson comorbidity index⁹⁴ and number of prescribed medications¹⁰¹ and non prescription medication, a history of depression and a previous diagnosis of depression.

*RAND 36-Item Health Survey 1.0 (RAND SF 36)*¹⁰⁰ is a measure of health related quality of life. The RAND SF 36 encompasses eight health concepts: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, general mental health, social functioning, energy/fatigue and general health perceptions. Reliability coefficients range from .65 to .94 across scales (median = .85)¹⁰².

*The Charlson comorbidity index (CCI)*⁹⁴ is a measure of risk of one-year mortality attributable to comorbidity. The CCI is also an indicator of disease burden and a method of predicting one-year mortality by weighting or classifying comorbid conditions. The following clinical conditions which are included in the CCI: myocardial infarction, congestive heart failure, peripheral vascular disease, dementia, cerebrovascular disease, chronic pulmonary disease, connective tissue disease, ulcer disease, moderate or severe liver disease, hemiplegia, moderate

or severe renal disease, diabetes mellitus, diabetes mellitus with end organ damage, any tumour, leukaemia, malignant lymphoma, malignant tumour, metastasis, AIDS.

Psychosocial data measured included measures of perceived social support as assessed by the Modified Social Support Survey -5 item version (MSSS-5)¹⁰³ and measures of strain related to informal care-giving as assessed by The Carers Strain Index¹⁰⁴. The MSSS-5 is an abbreviated version of the Modified Social Support Survey (MSSS) which is a multidimensional measure of perceived social support based on the Medical Outcomes Study¹⁰³. The MSSS-5 consists of the five items that correlate most strongly with the MSSS. This scale has a Cronbach α of .88¹⁰⁵.

*Carers Strain Index (CSI)*¹⁰⁴ is a measure of strain related to the provision of informal care. The CSI identifies potential areas of strain including: disturbed sleep, physical strain, financial strain, inconvenience, confinement, family adjustments, changes to personal plans, competing demands on time, upsetting behaviour, upsetting changes in the care recipient, work adjustments and feelings of being overwhelmed. This scale has a Cronbach α of .86.¹⁰⁴

3.3.6.2 The informal care exposure

Assessment of informal care giving exposure was based on the following questions: “Activities of daily living are the things we do during a typical day this includes any daily activity we perform for self-care (such as feeding ourselves, bathing, dressing, grooming), work, homemaking, and leisure. The following questions are about activities you might help the person that you care for do during a typical day. Which of the following activities do you provide regular help with?” A second question tapped into weekly exposure duration: “How many hours per week do you give help or support to the person that you care for?” For this question, participants could chose from the following categories: zero hours care provided per week, one to 19 hours care provided per week, 20 to 49 hours care per week and 50 hours plus care provided per week.

Four informal care exposure categories were established: zero hours care provided per week, one to 19 hours care provided per week, 20 to 49 hours care per week and 50 hours plus care provided per week.

Informal care activity during the study period was defined as providing a minimum of one hour help or support per week to a stroke survivor. The first notification of providing informal care (at three or six months follow-up) was used to classify informal care exposure during follow-up, i.e., study participants became exposed to providing informal care at the time that they stated that they provided a minimum of one hour care per week to a stroke survivor, or otherwise remained in the potentially exposed categories defined at baseline.

3.3.6.3 Outcomes

3.3.6.3.1 *Perceived stress (primary outcome)*

The primary endpoint for this study was the incidence of perceived stress recorded between the three month questionnaire up until and including the six month questionnaire. Psychological stress was measured using the Perceived Stress Scale (PSS)¹⁰⁶ Cases of stress were a score ≥ 23 . For details on how the clinical cut point was created see section 3.3.6.3.3 (Creation of a clinical cut point for perceived stress on the PSS) and section 3.3.6.3.4 (Methods for creating a clinical cut point on the PSS) below.

3.3.6.3.2 *The Perceived Stress Scale (PSS 10)*

The PSS 10¹⁰⁷ is a 10 item, global measure of stress. The PSS 10 assesses the degree to which situations within a persons life are appraised as stressful. An example on an item is ‘In the last month, how often have you been upset because of something that happened unexpectedly?’ (Item 1). Responses are recorded on a Likert Scale ranging from 0 = “never” to 4 = “very often”. The scale has a range of zero to 40. Scores are derived from the sum of the item scores with higher scores indicating a greater level of stress. The 10-item perceived stress scale measures perceived stress without losing any of the psychometric qualities compared with the 14 item version of the Perceived Stress Scale¹⁰⁸ and has good internal reliability ($\alpha = 0.78$) and construct validity.¹⁰⁷

3.3.6.3.3 *Creation of a clinical cut point for moderate perceived stress on the PSS 10*

The PSS 10 item measures stress on a continuous scale. There are no recognised thresholds for identifying cases of high stress for clinical practice and cut-points of clinical utility in this continuum to distinguish between individuals more or less affected by psychological stress. To create a threshold for high stress, a validated clinical cut-point on one similar scale was used as a reference to create a cut point on the PSS¹⁰⁶. To do this, raw Beck Depression Inventory II (BDI II)¹⁰⁹ and Perceived Stress scores from a study of 376 younger and older community dwelling adults was used¹¹⁰.

3.3.6.3.4 *Methods for creating a clinical cut point for moderate perceived stress on the PSS 10*

A BDI II score of 20 (representing moderate depression and when one would start to consider clinical intervention) was chosen. A BDI II score of 20 was found to lie on the 91st percentile of the data set. This was worked out by ranking the BDI II individual scores in the data set, then seeing how many observations were lower than or equal to the cut-off. The percentile was calculated using $100 * (\text{number lower} / \text{total } N)$.

BDI II = 356 people in total.

324 people score below 20.

$100 * (324/356) = 91\text{st percentile}$

The PSS 10 data was then ranked. The value that corresponded to the 91st percentile as the BDI II 20 clinical cut point to get the equivalent cut-point on the PSS.

PSS 10 = 372 people in total

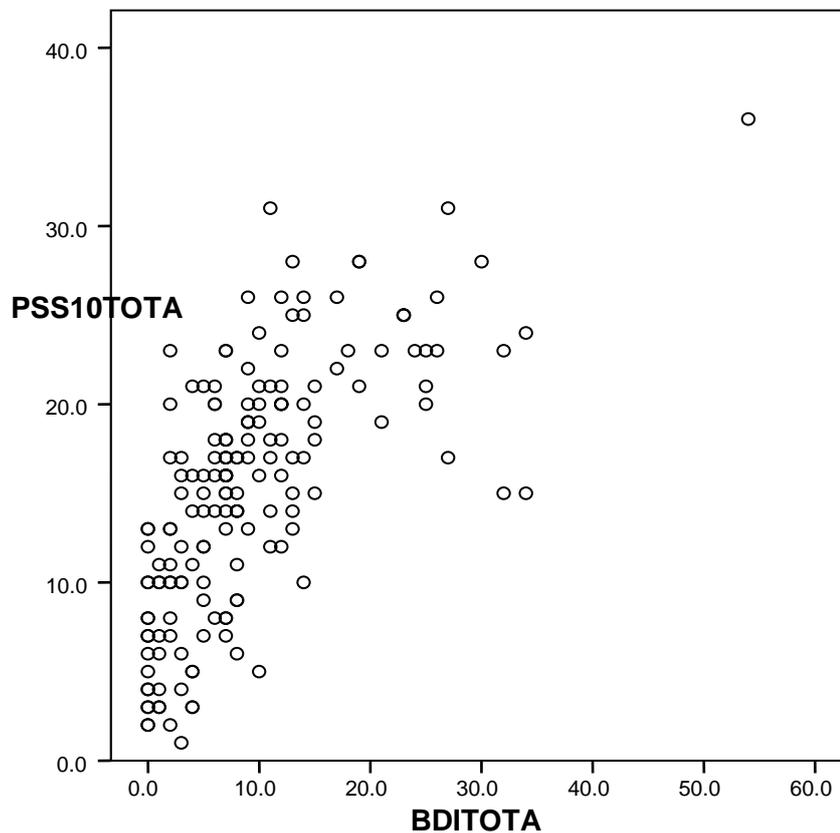
91st percentile

$(372 * 91) / 100 = 339 = \text{PSS 10 score of 23 for moderate stress.}$

For the purpose of this study the equivalent BDI II score of 20 is a PSS 10 score of 23. Therefore a score on 23 and above on the PSS 10 was taken to represent moderate stress.

3.3.6.3.5 *Spearman's Rank Order Correlation*

Spearman's Rank Order Correlation (ρ) is used to measure the monotonic relationship between two continuous variables¹¹¹. This analysis explores the relationship between perceived stress as measured by the PSS 10 and depression as measured by the BDI II. Spearman ρ (ρ) is the sample correlation coefficient (r_s) of the relative order (ranks) of data from the Beck Depression Inventory scores (BDI II)¹⁰⁹ and the Perceived Stress Scale scores (PSS 10)¹⁰⁶ from a study of 376 younger and older community dwelling adults¹¹⁰. The scatter plot of test (y axis) (figure 3.1) compared with standard has a significant, positive and strong rank correlation of 0.699 ($p < 0.001$, $n = 376$).



PSS 10 represents the Perceived Stress Scale 10 Item
BDI represents the Beck Depression Inventory II

Figure 3-1 Scatter plot $r = .699$. This is a scatter plot of Beck Depression Inventory scores (BDI II)¹⁰⁹ and the Perceived Stress Scale scores (PSS 10)¹⁰⁶ from a study of 376 younger and older community dwelling adults¹¹⁰. Each point in the scatter plot represents the values of the two variables (BDI II and PSS 10) for

any given participant observation. From this scatter plot it can be concluded that there is a strong and positive correlation between BDI II and PSS 10 scores. This is supported by Spearman $r = .699$.

3.3.7 Secondary outcomes

3.3.7.1 Somatic symptoms

Somatic symptoms are primarily physical complaints which do not have a medical explanation. Somatic symptoms are measured by the Patient Health Questionnaire (PHQ 15)¹¹². *The PHQ 15* is a 15 item somatic symptoms severity scale. The PHQ 15 is intended to function as a continuous measure of the severity of physical or 'somatic' symptoms. In addition, the PHQ assesses eight diagnosis divided into *threshold disorders* that is disorders that correspond to the Diagnostic and Statistical Manual of Mental Disorders IV¹¹³ (DSM-IV) diagnosis (major depressive disorder, panic disorder and bulimia nervosa) and *subthreshold disorders* (defined as having fewer symptoms than required for any specific DSM-IV diagnosis for example, other depressive disorder, other anxiety disorder). The PHQ is a self-report instrument composed of 15 physical symptoms including 10 of the diagnostic symptoms DSM-IV somatisation disorder. The PHQ symptoms are rated 0 ('not bothered at all'), 1 ('bothered a little') or 2 ('bothered a lot'). The scale has a range of 0-30, with higher numbers indicating a greater number of and severity of symptoms. High severity of symptoms is defined as a score of at least 15. The PHQ-15 has high internal consistency ($\alpha = 0.80$) and convergent and discriminant validity.

3.3.7.2 Psychological well-being

Psychological well-being was measured using the Oxford Happiness Questionnaire (OHQ) eight item scale¹¹⁴. The OHQ is an eight item scale selected from the original 29-item *Oxford Happiness Inventory*¹¹⁵, while maintaining acceptable reliability and validity¹¹⁴. The eight categories included in the OHQ short form are: feelings that life is rewarding, mental alertness, sense of satisfaction with self, ability to see beauty in things, sense of satisfaction with life, a sense of being personally organised, feelings of attractiveness and happy memories. An example of an item is 'I am well satisfied with everything in my life' (Item 3).

Responses are scored on a six-point Likert scale ranging from 1 = 'agree strongly' to 6 = 'strongly disagree'. Three items are reverse scored. Scores range from zero to 48 with higher scores indicating a greater level of psychological well-being.

3.3.7.3 Depression

Depression is measured by the Beck Depression Inventory II (BDI II)¹⁰⁹. The BDI II is a 21 item, self-administered test designed to assess intensity of depression. The 21 symptom attitude categories for the BDI-II measure include; sadness, pessimism, sense of failure, loss of pleasure, guilty feelings, punishment feelings, self-dislike, self-criticalness, suicidal thoughts or wishes, crying, irritability, loss of interest, indecisiveness, loss of energy, feelings of worthlessness, fatigability, sleep disturbance, irritability, loss of appetite, weight loss, difficulties concentrating and loss of libido. An example of an item is 'I don't cry anymore than I used to.' (Item 10). Respondents are asked to 'pick out one statement in each group that best describes the way that you have been feeling during the last two weeks, including today.' Each item has one numerical answer ranging from zero (low depression) to three (maximum depression). The BDI-II is scored by summing ratings given to each of the 21-items. The scale has a range of zero - 63. Cut-off scores for the BDI-II are: 0 to 13: minimal depression; 14 to 19: mild depression; 20 to 28: moderate depression; and 29 to 63: severe depression. Higher total scores indicate more severe depressive symptoms.

3.3.7.4 Case Fatality

Case fatality is defined as the number of participants dead at three months and at six months i.e., the end of scheduled follow-up.

3.3.7.5 Overview of questionnaires and measures

Table 3.1 Summarises the main GCCS measures that are collected at enrolment, three months and six months.

	Exposed participants	Non exposed participants
Baseline observation	Socio-demographic information CCI ⁹⁴ RAND SF-36 ¹⁰⁰ PSS 10 ¹⁰⁶ OHQ ¹¹⁴ PHQ 15 ¹¹² BDI II ¹¹⁶ History of depression Diagnosis of depression Health behaviours Number of prescription ¹⁰¹ and non prescription medications consumed Financial worries	Socio-demographic information CCI ⁹⁴ RAND SF-36 ¹⁰⁰ PSS 10 ¹⁰⁶ OHQ ¹¹⁴ PHQ 15 ¹¹² BDI II ¹¹⁶ History of depression Diagnosis of depression Health behaviours Number of prescription ¹⁰¹ and non prescription medications consumed Financial worries
Three month observation	Types of informal care activities performed Number of hours care provided per week PSS 10 ¹⁰⁶ OHQ ¹¹⁴ PHQ 15 ¹¹² BDI II ¹¹⁶ MSSS-5 ¹⁰³ CSI ¹⁰⁴ Number of prescription ¹⁰¹ and non prescription medications consumed Financial worries	PSS 10 ¹⁰⁶ OHQ ¹¹⁴ PHQ 15 ¹¹² BDI II ¹¹⁶ MSSS-5 ¹⁰³ Number of prescription ¹⁰¹ and non prescription medications consumed Financial worries
Six month observation	Types of informal care activities performed Number of hours care provided per week PSS 10 ¹⁰⁶ OHQ ¹¹⁴ PHQ 15 ¹¹² BDI II ¹¹⁶ MSSS-5 ¹⁰³ CSI ¹⁰⁴ CCI ⁹⁴ Health behaviours Number of prescription ¹⁰¹ and non prescription medications consumed Financial worries	PSS 10 ¹⁰⁶ OHQ ¹¹⁴ PHQ 15 ¹¹² BDI II ¹¹⁶ MSSS-5 ¹⁰³ CCI ⁹⁴ Health behaviours Number of prescription ¹⁰¹ and non prescription medications consumed Financial worries

Table 3.1 GCCS table of main variables collected at enrolment, three months and six months.

For details of exposed group three and six month questionnaires see appendices 12 and 13 respectively, for details of the non exposed group three and six month questionnaires see appendices 14 and 15 respectively.

3.3.7.6 Pre-testing the questionnaires

All the questionnaires were pre-tested¹¹⁷ to identify: words that were not clearly understood, questions that were ambiguous, questions that were upsetting, that close-ended questions had answers applicable to each participant, un-answered questions and that open ended questions elicited interpretable answers. Questionnaires were tested on a group of twenty people¹¹⁷ from different backgrounds: a selection of people accompanying stroke survivors to stroke clinic appointments and a selection of volunteers from the general public. The pre-testing questionnaire volunteers were asked to complete forms, length of time taken to complete questionnaires was noted. Once the questionnaire was completed the principal researcher had a debriefing session with individual respondents. This gave the principal researcher and respondent the opportunity, through informal interview, to identify questionnaire items with problems.

No changes were made to the structure of the questionnaires after pre-testing.

3.3.8 Procedures

After enrolment and completion of the baseline questionnaire, to maximise the response to the mail surveys, all cohort participants were called on the telephone giving advance notice that the questionnaire was about to be sent out at three and six months. All cohort study letters were personalized and signed in the same distinctive coloured ink. All mail-out envelopes containing the questionnaires were hand written in the same distinctive coloured ink, all stamps were placed on by hand. All mail-in envelopes were hand written in the same distinctive coloured ink and had the correct postage already placed on them. Participants who failed to return the questionnaires were called on the telephone a maximum of two times as a reminder.

3.3.9 Statistical analysis

The focus of this analysis was the relationship between exposure to providing care and incidence of perceived stress in people assessed as exposed to providing informal care at any time over the study period beginning at the three month questionnaire and ending at the six month questionnaire. All data were analysed in Statistical Package for the Social Sciences (SPSS V.15, SPSS). Baseline comparison of the exposed and unexposed groups was conducted using the χ^2 test or Fisher exact test, where appropriate, for categorical variables and the two sample t test for normally distributed continuous variables, and the Mann-Whitney test for non-normally distributed categorical variables. The primary endpoint of perceived stress and the secondary outcomes of psychological well-being, physical symptoms and depression were compared using both 2-sample t test and the Mann-Whitney U test for means and medians, respectively at three months and six months. Risk, difference, crude risk and odds ratios (OR) and adjusted odds ratios (OR) and 95% confidence interval were calculated for the primary outcome of perceived stress using binary logistic regression.

3.4 Results

3.4.1 Descriptive results

3.4.1.1 The exposed group

36 potentially exposed subjects consented to participate in this cohort study. One subject withdrew immediately after consenting to participate. Three subjects were excluded following screening. Two subjects withdrew immediately after baseline assessment and therefore their exposure to informal care status was not assessable. One participants care giving circumstances changed after consent and screening and before completion of the baseline questionnaire. One stroke survivor remained in hospital long-term during the period of the study. Therefore information was collected on informal care-giving activities from 28 participants at two time points over a six month period. See figure 3-2: flowchart of recruitment of participants who may become exposed to providing informal care.

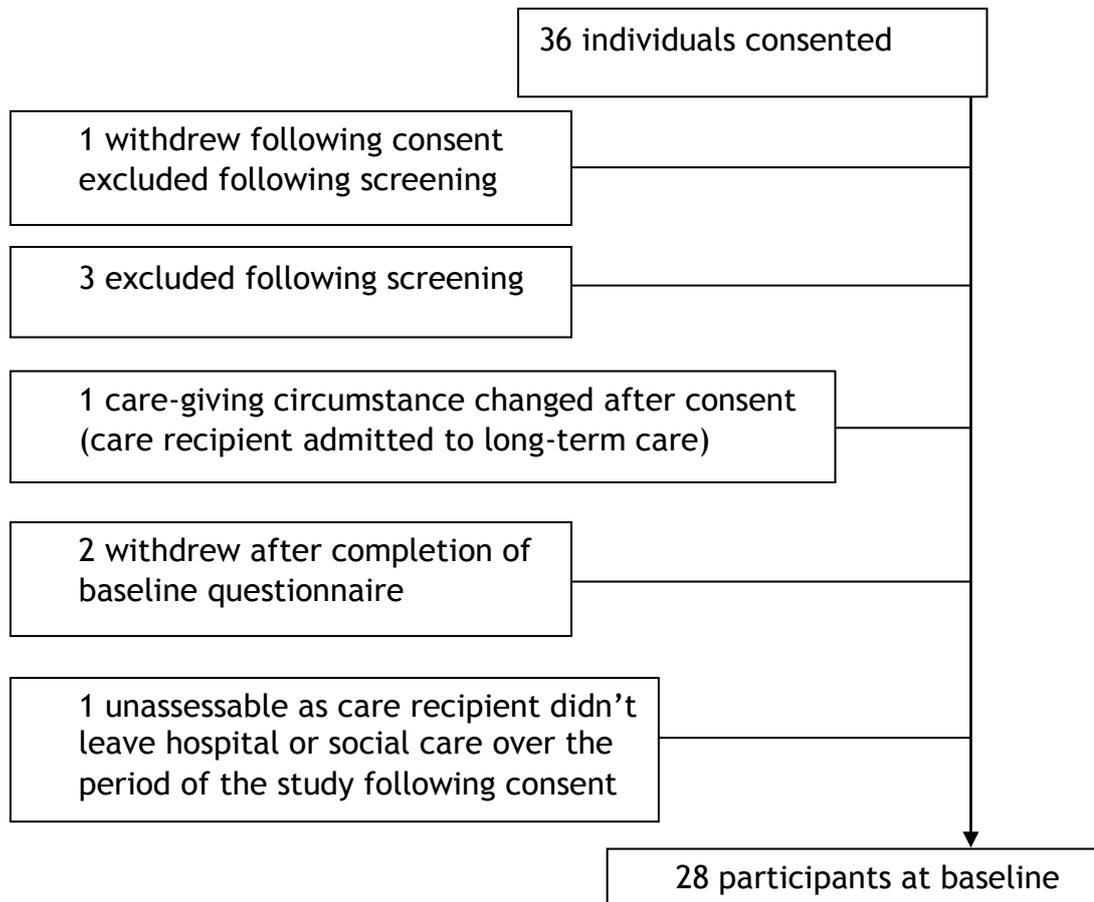


Figure 3-2 Flowchart of recruitment of participants who may become exposed to providing informal care.

3.4.1.2 Age sex matched unexposed participants

For details of recruitment of age sex matched unexposed participants see figures 3-3: flowchart phase 1 recruitment of reference group (the first attempt at recruiting age sex matched unexposed participants) and figure 3-4: flowchart phase 2 recruitment of reference group (the second attempt at recruiting age sex matched unexposed participants). For details of matching characteristics see table 3-2 matching characteristics.



Figure 3-3 Flowchart of phase 1 (first attempt) recruitment of reference group to GCCS.

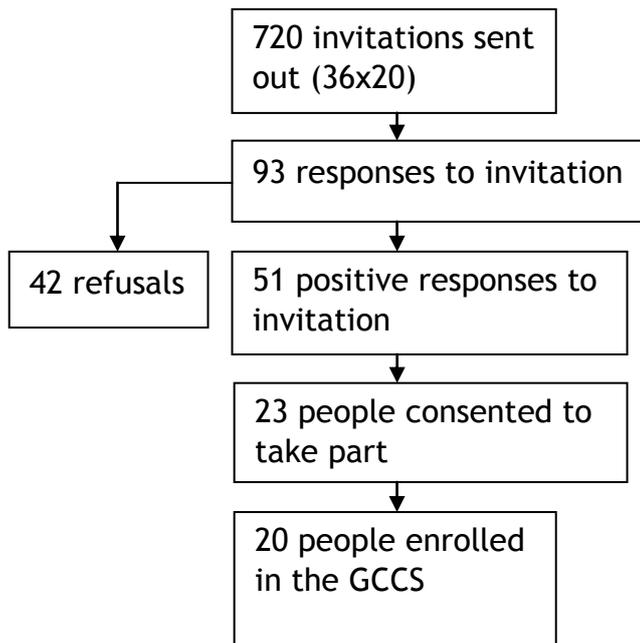


Figure 3-4 Flowchart of phase 2 (second attempt) recruitment of reference group to GCCS.

	Females		Males	
	Exposed group	Reference series (Unexposed)	Exposed group	Reference series (Unexposed)
Age	Age (yrs)	Age (yrs)	Age(yrs)	Age(yrs)
16-19	-	-	17	**
20-29	23	21		**
	26			
30-39	32	**	-	-
40-49	43	40	45	41
	42	40	-	-
	48	44	-	-
	49	47	-	-
	-	48	-	-
50-59	51	51	50	52
	52	52	53	52
	54	54	-	53
	55	50	-	53
	57	50	-	54
	-	56	-	56
	-	-	-	57
60-69	60	60	67	65
	61	60		65
	62	61	-	66
	64	61	-	68
	65	62	-	69
	65	62	-	69
	66	63	-	-
	67	65	-	-
	68	66	-	-
70+	71	70	*	70
	72	72	-	71
	-	-	-	78
	-	-	-	80
	-	-	-	81
	-	-	-	81

*denotes no exposed subject for matching ** denotes no available unexposed subject for matching

Table 3-2 Matching characteristics. Matching refers to the selection of unexposed participants (reference series) in the cohort study - that is identical or nearly identical, to the potentially exposed group (index series) with respect to age and sex, potentially confounding factors¹¹⁸.

3.4.1.3 Characteristics of the exposed and unexposed cohorts at enrolment

Mean age at enrolment was 53.1 years for the exposed group and 59.0 years in the unexposed group. There was a substantial difference ($p = 0.011$) in male/female split between exposed and unexposed groups, a key matching variable. At the time of recruitment there were higher levels of perceived stress as measured by the PSS-10, in the exposed group (mean difference (MD) 5.37 (95%CI, 1.19, 9.26, $p = 0.008$)), higher levels of non prescribed drug use in the unexposed group compared to the exposed group (MD)-.54 (95% CI -1.08, -0.004, $p = 0.048$). The Rand SF 36 scores for 'role limitations due to emotional problems', 'emotional well-being' and 'social functioning' were significantly lower in the exposed group compared to the unexposed group. There were no significant differences between exposed and unexposed groups at enrolment on the following measures: level of deprivation, economic activity, educational attainment, CCI scores, OHQ scores, PHQ 15 scores, BDI-II scores, numbers of prescribed medications, alcohol and tobacco consumption, history or diagnosis of depression or financial worries. See table 3-3 socio-demographic and lifestyle characteristics at enrolment and table 3-4 Baseline health characteristics at enrolment.

	Exposed	Unexposed	Statistical test	P-value
Sex	N = 28	N = 43		
Male	5(17.9%)	21(48.8%)	χ^2 test	0.011
Female	23(81.2%)	22(51.2%)		
Age	N = 28	N = 43		
Mean (SD)	53.1(14.6)	59.0(12.3)	2 sample t test	0.073
median 54.5 (IQR 45.9-65.1))		60.0(IQR 52.0-67.5)		
Marital Status	N = 28	N = 42		
Partnership	17(60.7%)	14(33.3%)	χ^2 test	0.073
Alone	9(32.1%)	23(54.8%)		
Widowed	2(7.1%)	5(11.9%)		
SIMD: 2009	N = 28	N = 43		
10	0	1(2.3%)	Mann-Whitney test	0.649
9	2(7.1 %)	1(2.3%)		
8	4(14.3%)	2(4.7%)		
7	3(10.7%)	8(18.6%)		
6	0	1(2.3%)		
5	1(3.6%)	2(4.7%)		
4	3(10.7%)	6(14.0%)		
3	5(17.9%)	2(4.7%)		
2	1(3.6%)	3(7.0%)		
1	7(25.0%)	17(39.5%)		
Economic activity	N = 27	N = 43		
Economically active	14(51.9%)	16(37.2%)	χ^2 test	0.228
Economically in-active	13(48.1%)	27(62.8%)		
Educational Attainment	N = 28	N = 43		
No qualifications	11(39.3%)	6(14.0%)	Mann-Whitney test	0.907
First level	4(14.3%)	10(23.2%)		
Second level	7(25.0%)	12(27.9%)		
Third level	6(21.4%)	15(34.9%)		
SMOKING				
History of smoking	N = 28	N = 42		
Yes	20(71.4%)	22(52.4%)	χ^2 test	0.111
No	8(28.6%)	20(46.6%)		
Current smoking activity	N = 28	N = 41		
Daily	10(35.7%)	12(29.3%)	χ^2 test	0.437
Occasionally	1 (3.6%)	0(0.0%)		
Not all	17(60.7%)	29(70.7%)		
Number of	N = 28	N = 41		

	Exposed	Unexposed	Statistical test	P-value
cigarettes consumed per day				
0	17(60.7%)	29(70.7%)	Mann-Whitney test	0.413
1-14	5(17.6%)	5(12.2%)		
15-24	4(14.3%)	5(12.2%)		
>25	2(7.1%)	2(4.9)		
ALCOHOL CONSUMPTION				
Frequency of alcohol consumption	N = 28	N = 43		
None	5(17.9%)	11(25.6)	Mann-Whitney test	0.706
Monthly or less	11(39.2%)	13(30.2)		
2 to 4 times per week	9(32.1%)	16(37.2%)		
4 or more times per week	3(10.7%)	3(7.0%)		
Amount of alcohol consumed on a daily basis, when drinking	N = 24	N = 32		
1 or 2	10(41.7%)	16(50.0%)	Mann-Whitney test	0.250
3 or 4	5(20.8%)	10(31.3%)		
5 or 6	5(20.8%)	4(12.5%)		
7 or 9	4(16.7%)	2(6.3%)		
OTHER WORRIES				
Financial worries	N = 26	N = 43	χ^2 test	0.870
Yes	4(15.4%)	6(14.0%)		
No	22(84.6%)	37(86.0%)		

SIMD represents Scottish Index of Multiple Deprivation.

Table 3-3 Socio-demographic and lifestyle characteristics of the exposed (index series) and unexposed (reference series) groups at enrolment to the GCCS.

	Exposed		Unexposed		Statistical test	P-value
	n	Mean (SD)	n	Mean (SD)		
Number of prescribed medications	28	2.6(2.6)	43	3.2(3.0)	2 sample t test	0.528
Number of non prescribed medications	27	0.3(0.8)	43	0.8 (1.2)	2 sample t test	0.048
PSS-10	28	16.2(8.3)	41	10.8(7.7)	2 sample t test	0.008
OHQ	26	31.6(6.4)	41	33.1(5.9)	2 sample t test	0.349
PHQ 15	21	6.8(4.6)	36	7.0(4.0)	2 sample t test	0.861
History of depression						
Yes	13	(46.4%)	22	(53.7%)	χ^2 test	0.555
No	15	(53.6%)	19	(46.3%)		
Diagnosis of depression						
Yes	10	(35.7%)	12	(29.3%)	χ^2 test	0.573
No	18	(64.3%)	29	(70.7%)		
	n	Median (IQR)	n	Median (IQR)		
BDI	25	8.00 (3.0-13.5)	36	8.5(4.25-14.5)	Mann-Whitney test	0.930
CCI	28	0(0-1)	43	0(0-1)	Mann-Whitney test	0.826
Rand SF 36						
Physical functioning	28	90.0 (65.0-100.0)	40	77.5(56.25-95.0)	Mann-Whitney test	0.119
Role limitations due to physical health	25	100.0(75.0-100.0)	36	100.0(75.0-100.0)	Mann-Whitney test	0.879
Role limitations due to emotional problems	26	83.3(0.0-100.0)	37	100.0(100.0-100.0)	Mann-Whitney test	0.017
Energy/ fatigue	28	55.0(30.0-75.0)	41	60.0(42.5-75.0)	Mann-Whitney test	0.458
Emotional well-being	28	70.0(44.0-83.0)	43	80.0(60.0-92.0)	Mann-Whitney	0.020

	Exposed		Unexposed		Statistical test	P-value
					test	
Social functioning	28	75.0(55.4-96.9)	43	100.0(75.0-100.0)	Mann-Whitney test	0.003
Pain	28	73.8(47.5-100.0)	42	80.0(56.9-100.0)	Mann-Whitney test	0.647
General health	27	70.0(40.0-80.0)	43	50.6(35.8-65.4)	Mann-Whitney test	0.856

PSS 10 represents Perceived Stress Scale
 OHQ represents Oxford Happiness Questionnaire (OHQ)
 PHQ 15 represents Patient Health Questionnaire
 BDI II represents Beck Depression Inventory II
 Rand SF 36 represents RAND 36-Item Health Survey 1.0
 CCI represents Charlson comorbidity index

Table 3-4 Health characteristics of the exposed (index group) and the unexposed (reference series) at enrolment to the GCCS.

3.4.2 Attrition

3.4.2.1 The exposed cohort

All participants took part in the data collection at three months. Two (7.7%) participants in the potentially exposed group did not return their self-administered questionnaires at six months.

3.4.2.2 Reference group

Of the 43 member of the reference group recruited at enrolment, 41 (95%) members of participated in the data collection at three months and 39 (90.7%) members participated at six months. One (2.3%) member of the reference group did not return their self-administered questionnaire at three or six months. One (2.3%) did not return their self-administered questionnaire at three months. Three (6.9%) did not return their self-administered questionnaires at six months.

3.4.3 First phase of follow-up (three month observation)

3.4.3.1 The exposed group

28 participants returned their self-administered questionnaires at three months. 24 participants of out 28 reported providing care giving activities at three months. Data on hours care provided per week was not completed by one participant. Three participants reported providing zero hours help and support to a stroke survivor at three months.

3.4.3.1.1 Types of care giving activities performed

Figure 3-5 shows the proportion of specific informal care giving activities undertaken as a percentage of all care-giving activities undertaken. Each segment represents a pre-specified category of informal care activity. Emotional support was the most frequently reported informal care activity at three months.

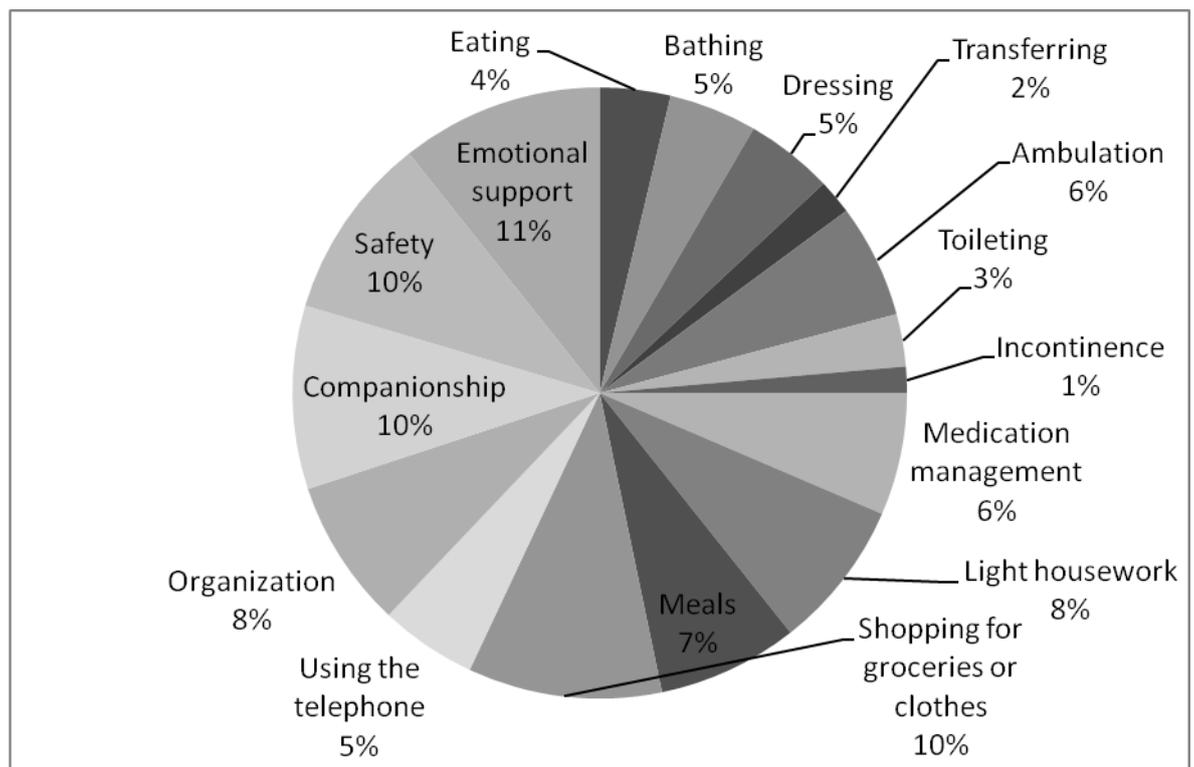
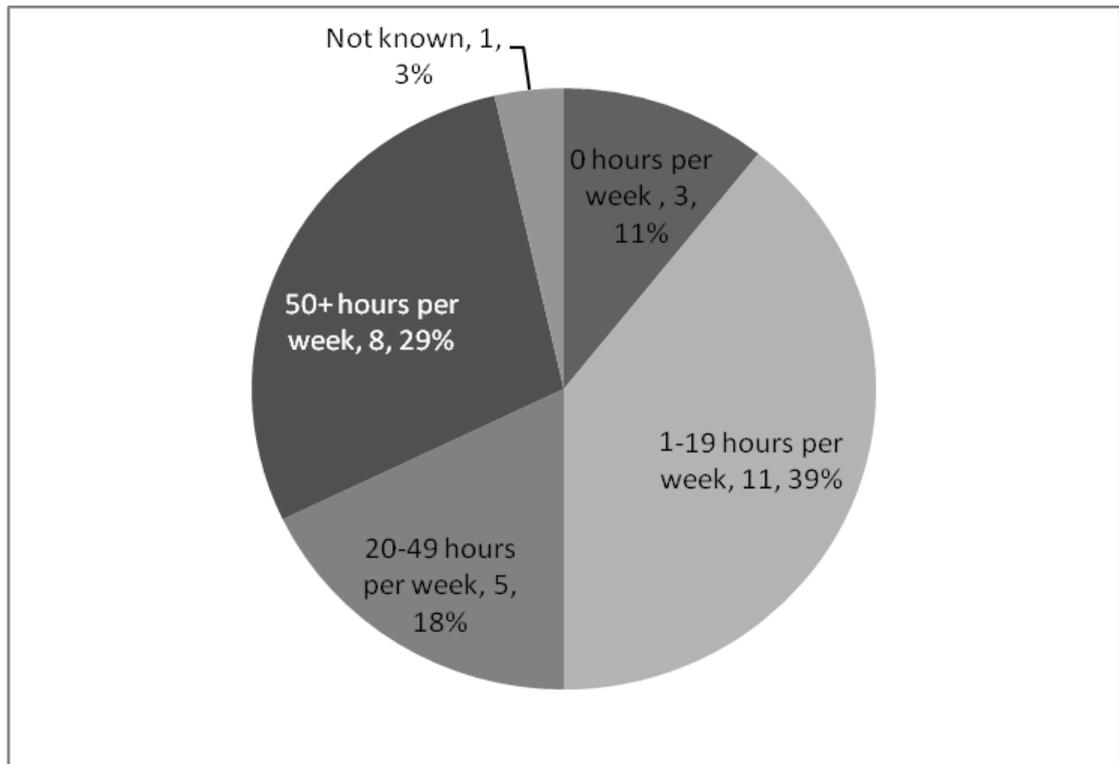


Figure 3-5 Type of care giving activity performed at three months as a percentage of all care giving activities at three months (n = 24).

3.4.3.1.2 *Levels of care giving exposure: number of hours care provided per week at three months*

One to 19 hours care per week was the most frequently reported category of informal care exposure with 11 (39%) participants reporting providing this level of informal care. Figure 3-6 provides information on the number (and percentage) of participants reporting each category of informal care exposure per week at three month (n = 28).



‘Unknown’ represents one person that did not complete the question on hours care provided per week.

Figure 3-6 Number (and percentage) of participants reporting each category of informal care exposure per week at three months (n = 28).

3.4.3.2 *Aspects of informal care giving which may give arise to stress or strain at three months*

The CSI¹⁰⁴ requires participants to respond to a list of ‘enduring problems that have the potential for arousing threat.’ intimating whether each item on the list is applicable to them. Figure 3-7 illustrates the percentage of exposed participants responding positively to each item on the CSI. Sixty-five percent of

respondents report being ‘completely overwhelmed (e.g., because of worry, concerns about how they will manage).

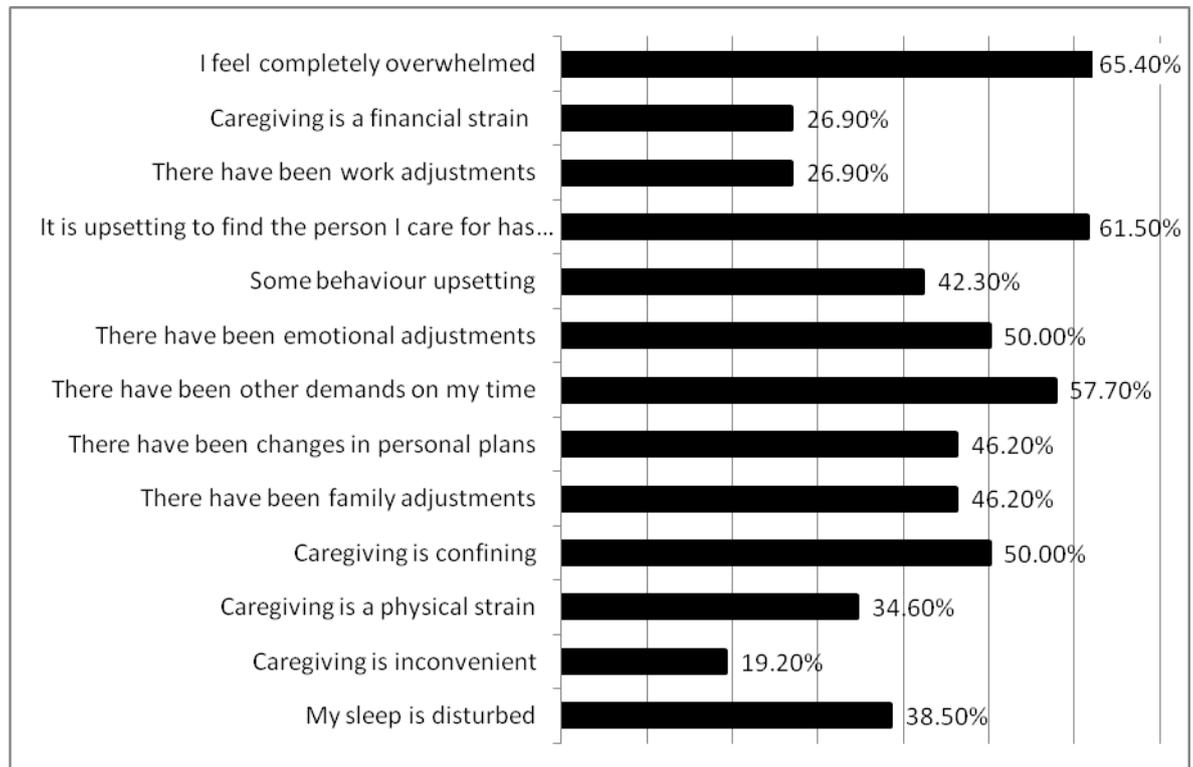


Figure 3-7 Aspects of informal care reported by exposed participants at three months as being difficult. Individual items are derived from and included in Carer Strain Index (CSI). The CSI is a measure of care giving related stress or strain. Data are presented as percentages (n = 24).

3.4.4 Socio-demographic, lifestyle, psychosocial and health data at 3 months

3.4.4.1 Social support data

There was no difference in level of social support as assessed by the MSSS 5 between the exposed (n = 27) and unexposed groups (n = 38) (exposed group median 65.0 (IQR 40-80.0) and unexposed group median 75.0 (IQR 45.0-91.25), p = 0.513).

3.4.4.2 Health data

There was no difference between the exposed groups at three months in either the number of prescribed and non prescribed medications.

	Exposed		Unexposed		Statistical test	P-Value
	n	Mean (SD)	n	Mean (SD)		
Prescribed medications consumed in previous month	28	3.1(2.92)	41	3.3(2.6)	2 sample t test	0.361
Non prescribed medications consumed in previous month	28	0.71(1.3)	41	0.785(1.1)	2 sample t test	0.788

Table 3-5 Health data at three months.

3.4.4.3 Financial worries at three months

There was no statistical difference between the exposed or unexposed groups with regards number of people with financial worries at six months (Table 3-7)

	Exposed	Unexposed	Statistical test	P-Value
Financial worries	N = 28	N = 39		
Yes	5(17.9%)	7(17.9%)	χ^2 test	0.992
No	23(82.1%)	32(82.1%)		

Table 3-6 Financial worries at three months.

3.4.5 Second phase follow-up (six month observation)

3.4.5.1 The exposed group

26 (out of 28) participants returned their self-administered questionnaires at six months. 24 participants out of 26 reported providing help or support to the stroke survivor that they care for at six months. Two participants reported providing zero hours help and support to a stroke survivor at three months.

3.4.5.2 Characteristics of informal care exposure at six month observation

3.4.5.2.1 *Types of care giving activities performed*

Of the 26 participants who returned their self-administered questionnaires at six months, 24 reported providing informal care to a stroke survivor. Figure 3-8 shows the proportion of specific informal care giving activities undertaken as a percentage of all care-giving activities undertaken at six months. Emotional support and companionship were the informal care activities most frequently reported by participants.

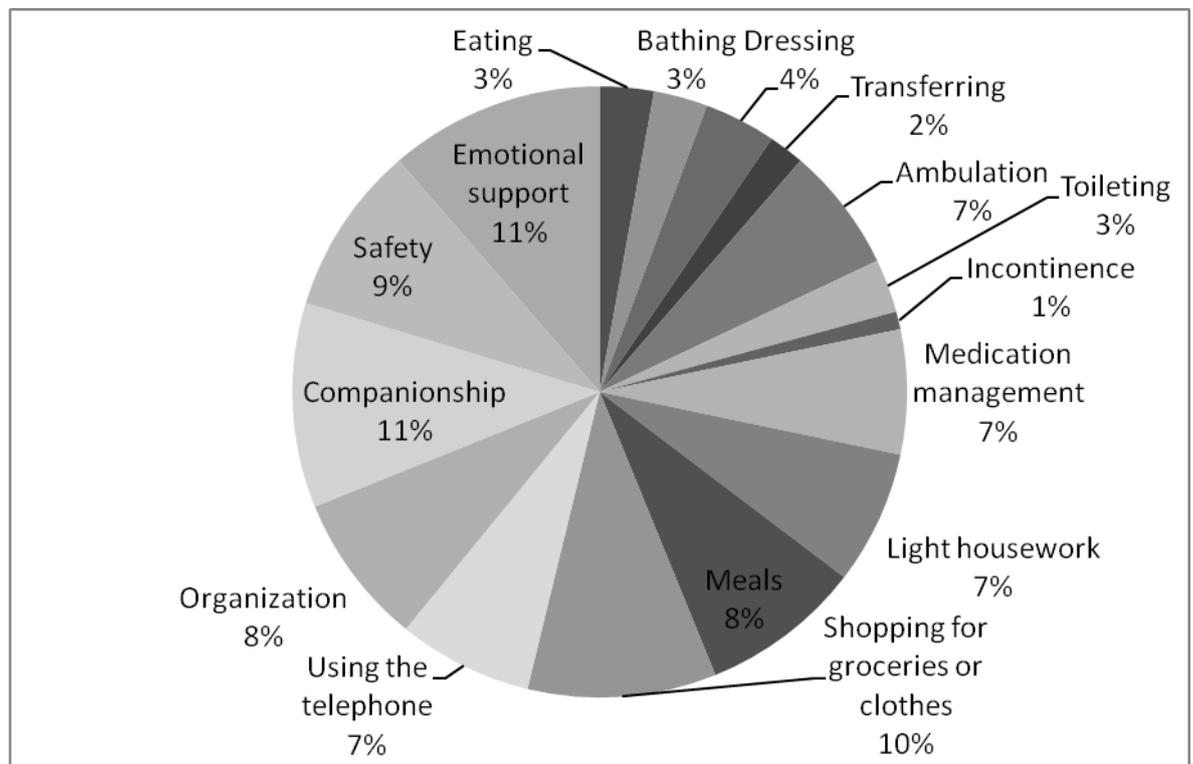
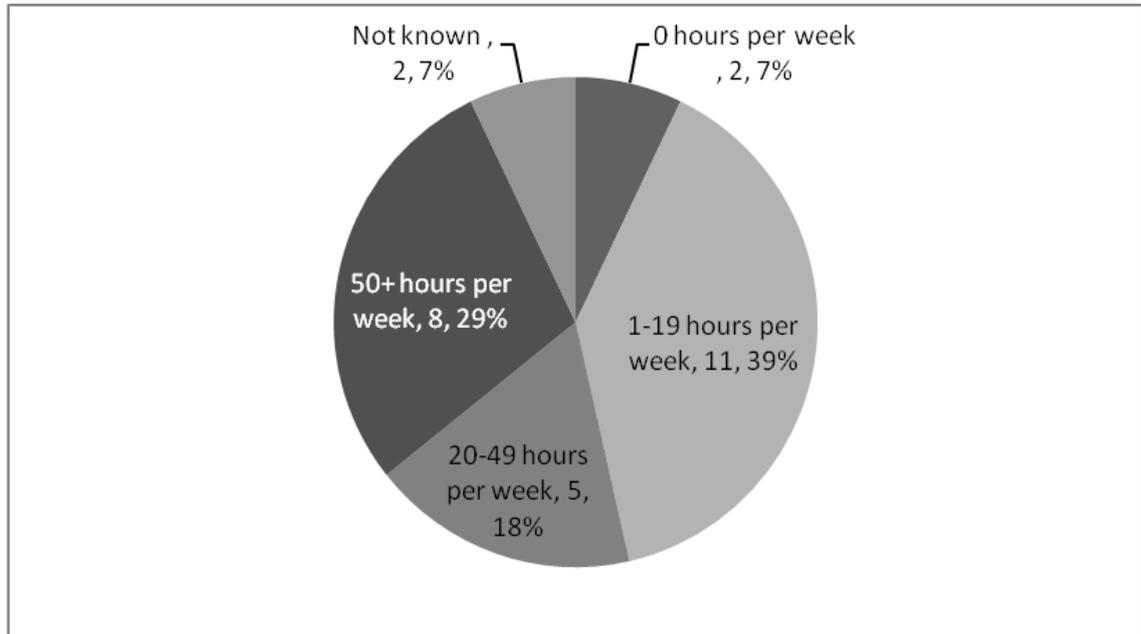


Figure 3-8 Type of care giving activity performed at six months as a percentage of all care giving activities at six months (n = 24).

3.4.5.2.2 *Levels of care giving exposure: number of hours care provided per week at six months*

One to 19 hours care per week was the most frequently reported category of informal care exposure with 11(39%) participants reporting providing this level of informal care. Figure 3-9 provides information on the number (and percentage) of participants reporting each category of informal care exposure per week at six months (n = 28).



Data not available for two people who did not return their self-administered questionnaires at six months.

Figure 3-9 Reported number of hours care provided per week provided at six months (n = 28).

3.4.5.3 Aspects of informal care giving which may give arise to stress or strain at six months (CSI)

Figure 3-10 illustrates the enduring problems identified by informal carers at six months enduring problems that have the potential for arousing threat to the informal carers. At six months 62% of people providing care to stroke survivors report that it is upsetting to find the person that they care for having changed so much.

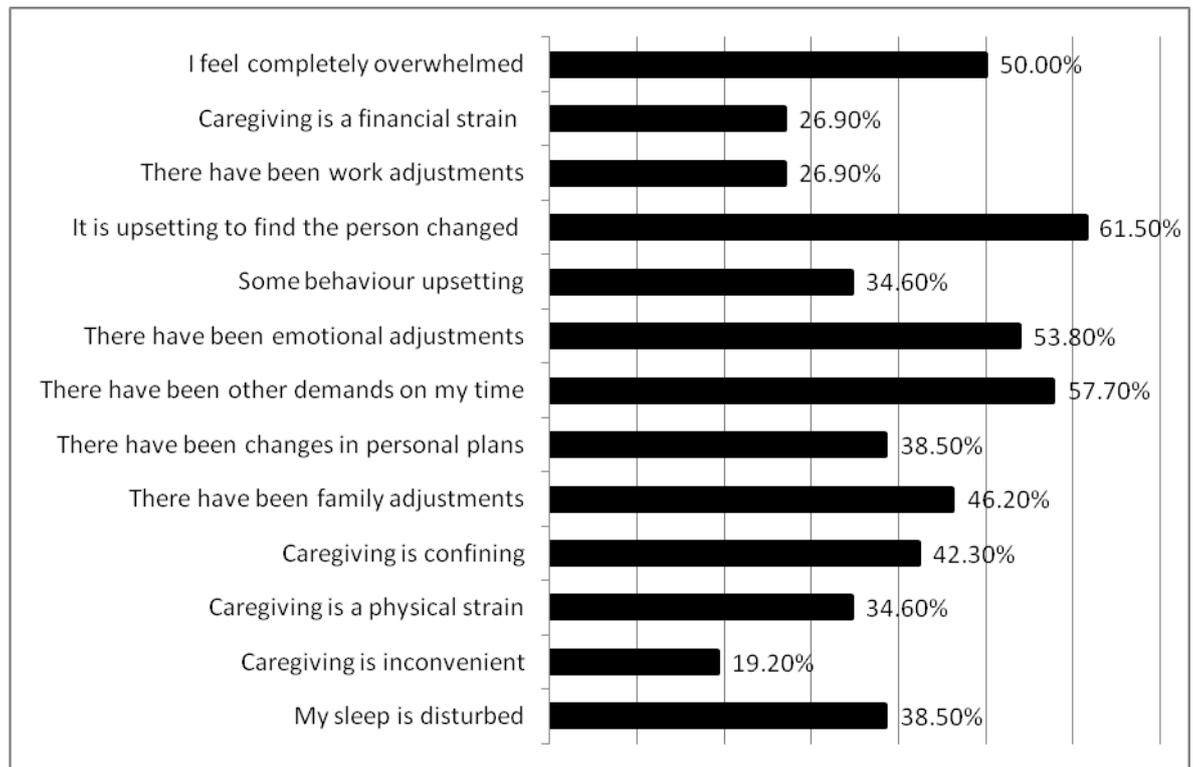


Figure 3-10 Aspects of informal care reported by exposed participants at six months as being difficult. Individual items are derived from and included in Carer Strain Index (CSI). The CSI is a measure of care giving related stress or strain. Data are presented as percentage (n = 24).

3.4.6 Socio-demographic, lifestyle, psychosocial and health data at six months

3.4.6.1 Social support data

There was no difference in level of social support as assessed by the MSSS 5 between the exposed (n = 26) and unexposed groups (n = 39) (exposed group median 65.0 (IQR 28.8- 81.25) and unexposed group median 70.0 (IQR 40.0-95.0), $p = 0.513$, $p = 0.397$).

3.4.6.2 Health data

There was no difference between the exposed groups at three months in either the number of prescribed and non prescribed medications consumed or CCI score. See table 3-7 for details.

	Exposed		Unexposed		Statistical test	P-Value
	n	Median (IQR)	n	Median (IQR)		
Prescribed medications consumed in previous month	26	2(0-4)	40	3.0(1.0-4.8)	Mann-Whitney test	0.600
	n	Mean (SD)	n	Mean (SD)		
Non prescribed medications consumed in previous month	26	0.9(1.2)	40	0.9(1.3)	2 sample t test	0.977
	n	Median (IQR)	n	Median (IQR)		
Charlson comorbidity index (CCI)	26	0(0.0-1.0)	39	0(0-2)	Mann-Whitney test	0.739

Table 3-7 Health data at six months.

3.4.6.3 Financial worries at six months

There was no statistical difference between the exposed or unexposed groups with regards number of people with financial worries at six months. See table 3-8 for details.

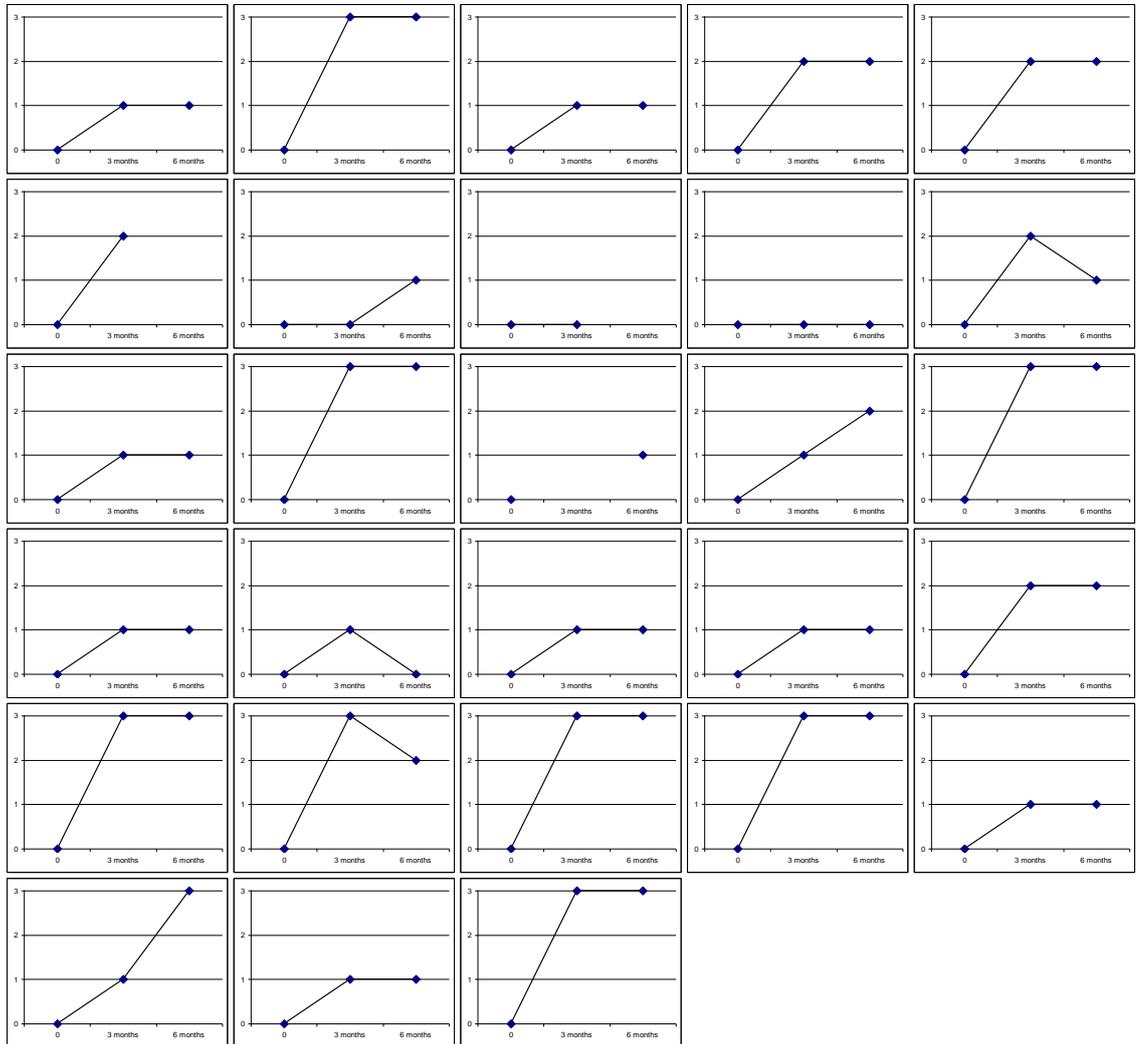
	Exposed	Unexposed	Statistical test	P-Value
Financial worries	N = 24	N = 37		
Yes	3(12.5%)	5(13.5%)	χ^2 test	0.909
No	21(87.5%)	32(86.5%)		

Table 3-8 Financial worries at six months.

3.4.7 Informal care exposure experience over time

Figure 3.11 illustrates each participants experience in different informal care exposure categories at three and six months. Informal care giving exposure experience is categorised as 0 hours per week, one to 19 hours per week, 20 to 49 hours per week and 50 plus hours per week. The individual graphs illustrate:

1) how the informal care exposure experience can vary over time 2) that it is possible for the exposure status to change from exposed to unexposed and vice versa and 3) that there are many possible informal care exposure sequences.



Time 0 = baseline. Categories of informal care exposure: 0 = no informal care exposure, 1 = 1-19 hours care provided per week, 2 = 20-49 hours care provided per week and 3 = 50+ hours care provided per week. Where data is available for all time points is represented by a continuous line joining each time point and equivalent category of informal care exposure.

Figure 3.11 Graphs of individual participants level of informal care giving exposure experience over time (n = 28).

3.4.8 Cross sectional effects at 3 and 6 months follow-up: stress responses and secondary outcomes

The primary purpose of this study was to assess the effects of providing care informal care to stroke survivors. At three months, 24 participants in the exposed group reported providing a minimum of one to 19 hours help or support to a stroke survivor. At six months, 24 participants reported providing a minimum of one to 19 hours help or support to a stroke survivor. It is important to note, that the 24 individuals who report providing care at three and six months are not all the same individuals at both time points. Table 3-9 presents the data on stress responses and secondary outcomes for 1) all participants recruited at baseline (n = 28) who had the potential to become exposed to providing informal care to a stroke survivor and 2) a sub group of participants who report providing a minimum of one to 19 hours help or support to a stroke survivor at 1) three and 2) six months.

3.4.8.1 Self-reported perceived stress in the subgroup of participants who report providing informal care at three and six months

Exposure to informal care was associated with higher levels of perceived stress in the group exposed to informal care (mean 16.8(SD 7.4) versus 9.9(SD 7.6), mean difference (MD) 7.0 (95% CI 3.4 to 10.6, $p < 0.001$) at three months and at six months MD 4.7 (95%CI 0.9, 8.6, $p = 0.017$). See table 3-9 for details.

The results for the subgroup do not differ substantially from the results of the main exposed cohort at three or six months. See table 3-9 for details.

3.4.8.2 Self-reported psychosomatic symptoms in the subgroup of participants who report providing informal care at three and six months

The subgroup exposed to providing informal care and the unexposed group did not significantly differ in mean scores of psychosomatic symptoms at three or six months. See table 3-9 for details.

The results for the subgroup do not differ substantially from the results of the main exposed cohort at three or six months. See table 3-9 for details.

3.4.8.3 Self-reported psychological well-being in the subgroup of participants who report providing informal care at three and six months

Exposure to care was associated with significantly lower levels of psychological well-being (happiness) in the subgroup exposed to providing informal care with MD -5.3 (95% CI-, -8.7,-1.9 p = 0.003) at three months and -5.7 (95%CI-8, -2.5, p = 0.001) at six months (Table 3-9).

The results for the subgroup do not differ substantially from the results of the main exposed cohort at three or six months. See table 3-9 for details.

3.4.8.4 Mortality

No deaths occurred in either group over the period of the study.

3.4.8.5 Self-reported depression in the subgroup of participants who report providing informal care at three and six months

The subgroup exposed to providing informal care and the unexposed group did not significantly differ in median scores of depression at three or six months. See table 3-9 for details.

The results for the subgroup do not differ substantially from the results of the main exposed cohort at three or six months. See table 3-9 for details.

	Recruitment			First observation (3 months)			Second observation (6 months)		
	n	Mean (SD)	P-value	n	Mean (SD)	P-value	n	Mean(SD)	P-value
Perceived Stress Score									
All 'exposed' recruited at baseline	28	16.2(8.32)	P = 0.008	28	17.0(7.1)	P < 0.001	26	16.0(8.7)	P = 0.017
Unexposed	41	10.8(7.7)		40	9.9(7.6)		39	10.9(6.9)	
<i>Subgroup exposed</i>				24	16.8(7.4)	P = 0.001	24	16.41(8.6)	P = 0.007
<i>Non exposed</i>				40	9.9(7.6)		39	10.9(6.9)	
Patient Health Questionnaire									
All 'exposed' recruited at baseline	23	6.8(4.6)	P = 0.861	20	8.9(6.2)	P =0.430	16	9.2(6.7)	P = 0. 524
Unexposed	36	7.0(4.0)		33	7.6(5.3)		17	8.0(3.4)	
<i>Subgroup exposed</i>				18	8.5(6.4)	P = 0.854	14	9.4(7.2)	P = 0. 496
<i>Non exposed</i>				33	7.6(5.3)		17	8.0(3.4)	
Oxford Happiness Questionnaire									
All 'exposed' recruited at baseline	26	31.7(6.4)	P =0.349	28	28.8(5.7)	P = 0.002	26	28.5(6.1)	P = 0.001
Unexposed	41	33.1(5.9)		38	34.2(7.1)		39	34.0(6.1)	
<i>Subgroup exposed</i>				24	28.9(5.9)	P = 0.003	24	28.3(6.2)	P = 0.001
<i>Non exposed</i>				38	34.2(7.1)		39	34.0(6.1)	
	n	Median (IQR)			Median (IQR)			Median (IQR)	
Beck Depression Inventory									
All 'exposed' recruited at baseline	25	8.0(3.0-13.5)	P = 0.930	25	14.0(5.5-18.0)	P = 0.600	25	10(5-15.5)	P = 0.246
Non exposed	36	8.5(4.3-14.5)		34	7.5(3.75-13.0)		36	7.0(3.3-15.3)	
<i>Subgroup</i>				22	14.5(5.0-13.0)	P = 0.105	23	12.0(6.0-16.0)	P = 0.139
<i>Non exposed</i>				34	7.5(3.75-13.0)		36	7.0(3.3-15.3)	

Table 3-9 Cross sectional effects at 3 and 6 months follow-up: stress responses and secondary outcomes. Data presented are results for 1) all participants recruited at baseline (n = 28) who had the potential to become exposed to providing informal care to a stroke survivor and 2) a sub group of participants who report providing a minimum of one to 19 hours help or support to a stroke survivor at three and six months. Grey shaded bold area represents the results for a subgroup of exposed participants who have intimated that they are providing informal care to a stroke survivor at three or six months.

3.4.9 Quantification of the association between informal care exposure and perceived stress

Over the period of follow-up, 26 individuals reported providing informal care to a stroke survivor at one or both time points.

The primary endpoint is incident cases of psychological stress; that is the number of people who score ≥ 23 on the PSS.

	Exposed	Not exposed	Total
Perceived stress ≥ 23	9	2	12
Perceived stress ≤ 22	16	37	52
Totals	25	39	64

Table 3-10 Results of matched cohort study of perceived stress (primary outcome) among participants who were 'exposed' or 'not exposed' to providing informal care to stroke survivors.

Observed counts: GCCS

Incidence proportion = the proportion of people who score 23 or over on the Perceived stress scale at any time over the six month study period.

3.4.9.1 Difference measure: Risk difference

The risk difference (RD) is the absolute difference between the proportion of events between the two comparison groups (exposed and unexposed). The RD measures change on an additive scale. If $RD > 0$, then the informal care exposure is associated with an increase in the probability of stress; if $RD < 0$, the informal care exposure is associated with a decreased probability of stress; if $RD = 0$, then exposure to informal care is not associated with stress¹¹⁹.

$$\text{Exposed} = 9/25 = 0.36$$

$$\text{Unexposed} = 2/39 = 0.0513$$

Risk difference = $0.36 - 0.0513 = 0.3087$ or 31% (95% CI 11% to 51%, $p = 0.003$).

Therefore, exposure to informal care is associated with an increase in the risk of stress.

3.4.9.2 Ratio measures: risk ratio

The risk ratio is the ratio of the risk in the exposed group to the risk in the control group. The risk in this instance is the proportion of subjects who have scored ≥ 23 on the Perceived Stress Scale (an event) in the exposed group to the total in the group. RR is on a multiplicative scale. If $RR > 1$ then the informal care exposure is associated with an increase in the probability of stress; if $RR < 1$, the informal care exposure is associated with a decreased probability of stress; if $RR = 1$, then exposure to informal care is not associated with stress¹¹⁹.

Risk ratio = Incidence proportion Exp/ Incidence proportion UnExp = $0.36 / 0.0513 = 7.02$ (95% CI 1.65 to 29.85, $p = 0.002$)

A risk ratio of 7.02 indicates that the risk in the group exposed to informal care is 7.02 times that of the non-exposed group. The segment of the risk ratio above 1 quantifies the relative increase (or decrease) in risk associated with exposure. Therefore, a risk ratio of 7.02 reveals a 600% increase risk of stress with exposure to informal care.

3.4.9.3 Ratio measures: odds ratio

The odds ratio (OR) is the ratio of the odds of an event (stress) in the exposed (informal care) group to the odds of an event in the unexposed group. In this instance, odds are the number of people in either the exposed or unexposed group with an event to the total people in that group. OR is on a multiplicative scale. If $OR > 1$ then the informal care exposure is associated with an increase in the odds of stress; if $OR < 1$, the informal care exposure is associated with a decrease in the odds of stress; if $OR = 1$, then there is no difference between the exposure and non exposed groups¹¹⁹.

Odds ratio = odds in group exposed group ($9/16 = 0.565$) / odds in unexposed group ($2/37 = 0.0541$) = 10.41 (95% CI 2.02 to 53.68).

An odds ratio of 10.41 indicates that people who are exposed to providing informal care to stroke survivors have 10.4 times the odds of being stressed compared to people who are not exposed to providing informal care.

The adjusted odds ratio (adjusted for baseline stress, age and sex) is 6.26 (95%CI 0.94 to 41.41, $p = 0.058$).

It was not possible to expand the investigation to include other covariates because of the small sample size.

3.5 Discussion

Previous studies have highlighted family care giving stress as a significant psychological risk factor. However, it is worthwhile taking a close look at the evidence which underpins this belief. One major study²⁹ is cited regularly as evidence of the stressful effects of providing informal care. This study examines the relationship between informal care to older disabled spousal partners and four year all cause mortality. This study is an ancillary study of a larger well established prospective cohort study; the Cardiovascular Health Study¹²². This study compared people who provide care to a non-care giving reference group. Care-giving status was established using a simple yes or no question about care-giving activities that were currently undertaken. Stress was measured using a self-report measure of stress (using three pre-defined levels; 'no', 'some', 'a lot of strain') associated with particular care giving activities rather than a more objective measure, such as the PSS. Therefore, this study is at risk of high false positives. Moreover, this study examines the risk of 4 year all cause mortality; it is not designed to examine the risk of stress in exposed care giving and unexposed non care giving groups. Rather it examined the strength of association between self-reports of stress and the primary outcome. This raises several issues. First, observed associations generated from analysis involving evaluation of possible associations (such as the relationship between subjective stress assessment and 4 year all cause mortality) do not necessarily indicate a causal relation between these variables. Second, investigators and journals are more likely to publish 'interesting' (publication bias) or statistically significant positive associations, even if they are false positives. Lastly, care-giving status

and covariates were assessed at baseline and analytic methods were used to model their effects on mortality on average 4.5 years from baseline. It is clear from the results of this study that the informal care exposure is not an *easily identifiable, easily measurable or permanent condition*⁴³⁷.

As far as is known, the Glasgow Carers Cohort Study is the first cohort study designed to investigate the causal relationship between exposure to providing informal care to a stroke survivor and perceived stress.

In this study, it has been demonstrated that there is an increase in risk of perceived stress of somewhere between 165% and 2985% with the best estimate of increase being 700% within six months of being exposed to providing informal care. The mean level of stress is also significantly higher in people who are exposed to providing informal care compared to non exposed individuals. However, the confidence intervals are wide reflecting the small sample size. It was not possible to determine neither whether the incidence of stress increased with the amount of care provided increased nor whether to examine whether the increase in stress was due to factors other than exposure to providing informal care because of the small sample size.

It is possible, however, that these findings are due to confounding by unknown or unmeasured physiological, psychological, behavioural and socioeconomic factors related to both the informal care exposure and to health outcomes. In observational studies such as this one, informal care exposure is related to numerous known and unknown confounding factors; ill health may inhibit a persons ability to promote the welfare of another, equally people may misreport the intensity or duration of their informal care-giving activities, making interpretation if observed associations between exposure to informal care and adverse health outcomes difficult. However, it is highly unlikely that the definitive test of a causal relationship - the randomised controlled trial of the long-term effects of promoting the welfare of another in sickness or disability will ever be performed. However, in an attempt to increase the efficiency of confounder control and thereby *increase the precision of the confounder-adjusted estimate* a matched study design has been used¹¹⁸. The purpose of the matched design is to ensure that unexposed (referent) participants are selected in a way that forces the distribution of covariates to be similar in the exposed

and referent (unexposed) group. However, it was not possible or practical to select the unexposed cohort on all prognostic factors for the primary outcome of stress such as level of deprivation (as determined by the Scottish Index of Multiple Deprivation (SMID) deprivation data zones). Moreover, matching is only one of several methods to deal with confounding. For example, if the dataset had been of sufficient size, confounding could have been addressed by adjustment in a regression model with the informal care (exposed) group and confounding variables such as deprivation score, used as explanatory variables.

An important factor which needs to be taken into consideration is people who are exposed to providing informal care appear to be exposed to at least two component factors which may have a causal action which leads to stress. The first is exposure to providing informal care. The second is the experience of having a relative, friend or other experience a serious illness and is hospitalized for that illness. We have excluded participants from this study who have had significant informal care responsibilities prior to this single episode. Ideally, in a cohort study, two groups of people should be identified who are free of 'disease' or in this case stress and that differ with regards to the extent of their exposure to informal care. The potentially exposed people who were recruited to this study were not free of 'stress' at baseline. Therefore, the apparent effect of exposure to informal care appears to be distorted because of the '*profound sense of shock and disorientation*' that occurs when the worst happens - '*a death in the family, a terrorist attack, an epidemic of virulent disease...*'¹²³ ***a stroke in the family***. What is not clear is whether the stress and melancholy observed in this study is due to the traumatic event i.e., stroke and other stroke related sequelae (for (example grieving for the pre-stroke personality, loss of income) or due to the need to provide informal help and support or both. Moreover, the subgroup analysis at three and six months shows that the findings remain unchanged when the analysis is extended to include all potentially participants enrolled at baseline. Which adds to the argument that what may have been measured are the consequences of a shocking event - a stroke in the family. It is also worth noting that the definition of informal care used in this study appears to have been open to interpretation by participants. This is best illustrated by noting that participants who intimated that they did not provide help or support to a stroke survivor, all responded that they found

providing care 'overwhelming' on the Carer Strain Index. This raises the issue of the need to separate 'one who cares' from one 'who provides what is necessary for the health, well-being, maintenance and protection of an individual in ill health, frailty or disability'. In other words, it is important to separate out the '*profound sense of shock and disorientation*' that occurs when there is a stroke in the family from the effects of having to continuously promote the welfare of another in illness, disability or frailty on a long term basis. One can never prevent bad things happening to people. The effect of working continuously to promote the welfare of another in ill health, frailty or disability is a separate issue.

This research was designed, conducted and analysed based on the assumption that the informal care exposure groups were defined and fixed at the start of follow-up, which is a fixed cohort, with no movement of participants between exposure groups at follow-up. The focus was the average risk of perceived stress over the time at risk of informal care exposure effects (from the start of the six month exposure interval).

One of the most important features of the informal care exposure that has come to light in this study is that the identification of study cohorts of informal carers is not simple process of classifying participants as to their informal care exposure status. The informal care exposure is not a permanent condition. Cohorts of individuals who provide informal care are not fixed like the groups defined by randomisation and treatment allocation in randomised controlled trials. Different individuals can experience different informal care exposure levels at different times. It is possible for one individual to have a unique sequence of informal care exposure levels and therefore it is possible to create one unique informal care exposure cohort including only that one individual. The approach taken in this study has been to simply treat the informal care exposure as continuous, individuals have been classified into broad categories of exposed and not exposed based on their intimation of care provision at three and six month follow-up on one of four pre-defined ordinal response categories of response (zero hours per week, one to 19 hours care, 20 to 49 hours care per week and 50 plus hours care per week). This raises several issues. First, this simple approach fails to take account of the need to classify the informal care experience of a single individual in different exposure categories at different

times. Second, the study has not been designed to measure the amount or dose of informal care as it relates to the causation of perceived stress. Ideally, the data collected should have been duration of informal care exposure (number of weeks providing care) and intensity of informal care exposure (number of hours provided per day or per week). However, direct calculation of incidence rates within categories of informal care exposure would require a much larger study population in each informal care exposure category than is available in this study, if the incidence rates are to be statistically stable. Third, using pre-defined ordinal categories of informal care exposure has significantly reduced flexibility in data analysis. Collection of data as numerical values, for example, participants estimated number of hours of informal care provided per day (or per week) would have allowed a much more flexible approach to defining the informal care exposure categories and data analysis. Furthermore, this simple measure of the amount of informal care provided per week may not be sufficient to measure the amount of exposure as it relates to any adverse health endpoints and therefore this study may be susceptible to substantial measurement error leading to a lessening of the magnitude of the informal care - adverse health endpoint association than has been demonstrated.

At the outset of this study there was no basis for hypothesizing a specific induction period between exposure to informal care and psychological stress response (the primary outcome), that is the interval from exposure to providing informal care to the psychological stress response as measured by the PSS 10. However, it was assumed based on the concept of the origins of carer stress or strain, that if exposure to providing informal care is a distressing psychological stimuli, in that exposure is perceived to be threatening, harmful or challenging to any aspect of the informal carers 'self' (for example sleep is disturbed, care recipients behaviour is upsetting, competing demands on time, physical strain) then the stress response is likely to occur immediately and simultaneously with the perceived threat that is, the informal care exposure. Therefore, for the purpose of estimating informal care exposure stress effects in this cohort study it was assumed that the induction period was close to zero. That is the perceived stress effects of exposure to providing informal care are hypothesised to be contemporaneous with the exposure. Therefore, participants are at increased risk of stress only during the time that they are exposed to providing

informal care; therefore time exposed to providing informal care is time at risk. However, the induction period (i.e., time from causal action to onset of adverse health outcome) is likely to vary depending on the adverse health outcome of interest (such as depression) and vary for individuals. Therefore, lack of evidence of the informal care effect on the symptoms of depression may be due to insufficient time (or follow-up) to allow the informal care exposure experience to accumulate or the effects to develop.

The objective of this study was to recruit all available potential carers of stroke survivors who were eligible to participate on a strict consecutive sampling basis and to recruit a random sample of age sex matched unexposed subjects. However, the use of external agencies (SSRN and SPCRN) to recruit to the GGCS made it difficult to determine the proportion of people in the GRI stroke service acute stroke admissions sampling frame and the General Practice sampling frame who were eligible to participate (response rate) as no data were available on the number of people who either refused screening or were never reached. The reasons why target sample size was never reached was that the GGCS was in competition with other studies for time from the SSRN staff. Moreover, recruiting to the GGCS required SSRN staff to be available on the stroke units at visiting times; therefore the time window of opportunity for recruitment was limited. On the other hand, visiting times offered the greatest concentration of potential recruits. In addition, it is not known how many potential carers of stroke survivors who were screened for eligibility but refused to participate. However, it is known that the non response rate in the general practice sampling frame was high as only a small proportion of screening invitations were responded to. Failure to reach a subject and refusal to participate is likely to introduce selection bias, particularly given that participation in this study could be influenced by both adverse health outcomes and exposure status. For example, people who are in ill health or have experienced ill health may be more willing to provide help and support to another in ill health or disability for reasons of reciprocity, to feel better about themselves, to demonstrate kindness and generosity.

The complex and involved nature of the identification, recruitment and follow-up process, while protecting potential and eligible study subjects, has introduced a number of potential points of failure in the overall execution of the

study. For example, recruitment of an age sex matched unexposed subject required five contacts before a participant could be screened for eligibility. Indeed, the methods that were used in this study have been shown to actively reduce response rates, specifically the 'opt-in' procedures for the unexposed cohort. In addition, as the original mail outs were handled by the SPCRN, no information was available to the principal investigator on those who did not respond. Therefore, it was not possible to increase the response rate by sending out multiple mailings to non -respondents. However, this may have been deemed inappropriate by the ethics committee.

3.6 Conclusions

The results of this cohort study are not conclusive. Nevertheless, they provide stronger evidence than previous studies that exposure to providing informal care to stroke survivors' affects levels of perceived stress and levels of psychological well-being. The fact that the level of perceived stress remained constant from recruitment and over follow-up, despite the change in care-giving circumstances, makes it difficult to disentangle the stress effects of having a close friend, relative or loved suffer a stroke from the stress effects of providing practical support and help to that individual when they return to live in the community. However, regardless of the origin of the stress, it is important to note that there is significantly more stress in a group exposed to providing care to stroke survivors in the first six months after hospital discharge. Interestingly, the results of this research appear to demonstrate a temporal relationship between exposure to providing informal care and lower levels of psychological well-being or happiness. The lower levels of happiness observed in the exposed group may equate to milder levels of depression observed in some studies. This study did not find significantly different levels of depression between the exposed and unexposed groups. Further research should look at the long term implications of the stress response observed in people who provide informal care, at the long term effect of exposure to providing informal care and examine further underlying mechanisms.

3.7 Implications for practice

Health and social care professionals should be aware that people who provide care to stroke survivors may perceive their life to be stressful. At present (see Chapter 5) there is insufficient evidence to support the use of any non-pharmacological interventions designed to promote a persons ability to cope in the role of care giver. Arming people with the necessary knowledge, skills and abilities take on the care giving role beforehand may or may not work⁶³. Health and social care professionals are encouraged to make available information on resources such as the Princess Royal Trust for Carers.

3.8 Implications for research

The findings from this study are considered preliminary until confirmed and refined by other research.

The epidemiological model described above provides a starting point for defining and examining the effects of the informal care exposure. However, in this study and in general, informal care is not a well-defined construct. Therefore, every effort needs to be made to develop a substantively meaningful conceptualisation of the informal care exposure which will provide the foundations for the design of cohort studies and the analytic approach taken. Future research needs to:

- Take account of the complex time-varying chronic nature of the informal care exposure and the need to classify different people in different informal exposure categories at different times.
- Consider the possibility that the informal care exposure experience may accumulate over time.
- Focus on the development of an operational definition of the informal care exposure that can be measured⁴⁴⁰.
- Identify the best method to represent the informal care exposure dose as it relates to adverse health outcome causation⁴⁴⁰.
- Identify the period of time during which informal care exposure is likely to cause the outcomes of interest⁴⁴⁰.

- Works towards developing an algorithm which can be used to calculate the informal care exposure dose variable over the critical time period that will be used in the statistical analysis of any future epidemiological study of the effects of informal care⁴⁴⁰.

Chapter 4 Incidence, prevalence and association between providing informal care-giving to stroke survivors and depression: a systematic review and meta-analysis.

4.1 Introduction to chapter

Health care professionals and the lay public alike associate providing informal care and depression. However, the cohort study described in Chapter 3 failed to find a significant difference in levels of depression between those who were exposed to providing informal care compared to those who were unexposed (RR 0.87 (95% 0.3, 2.50, $p=1$). There may be several reasons for this. First, the cohort study was not designed or powered to detect significantly different levels of depression between the care-giving (exposed) and non-care-giving (unexposed) groups as incidence of depression was not the primary end point. Second, depression may be the result of cumulative experience of exposure to providing informal care over a longer period of time than six months and therefore, the cohort study was not of sufficient length to allow depression to develop in people who provide care to stroke survivors. Finally, there may be no real difference in the level of depression experienced by people who are exposed to providing care compared to those not exposed to providing care. Nevertheless, depression in people who provide care to stroke survivors is a major concern for policy makers, the public, informal carers and health care professionals. Therefore it is important that the results of the cohort study discussed in Chapter 3 are placed in the context of previous studies.

4.2 Background

4.2.1 *The epidemiological study of informal carers*

The goal of epidemiologic research in informal carers is to obtain valid and precise estimates of the effect of exposure to providing informal care (the potential risk factor) on the occurrence of conditions of interest, in this case depression. In other words, epidemiological research is the means to finding risk factors for depression and exposure to providing of informal care is a possible candidate.

4.2.2 *Measures of occurrence*

In epidemiological research there are four basic measures of disease occurrence: prevalence, incidence times, incidence rates and incidence proportions¹²⁴. Prevalence of depression is the most frequently reported measure of disease frequency in informal carer research. Prevalence represents the proportion of the population of people who provide informal care with depression at a specified time and reflects both the incidence rate and the duration of depression. While prevalence data are useful for planning health resources and facilities, they do not tell us whether depression occurs as an effect of providing informal care. To study causes, it is more useful to measure the incidence rate (the occurrence of new cases of depression per unit of person time¹²⁴) or incidence proportion (the proportion of people who develop new depression over a defined period¹²⁴) than prevalence of depression. To determine if exposure to providing informal care to a stroke survivor is a cause of depression, it is necessary to demonstrate an increased incidence of depression in people who are exposed to providing informal care (exposed) to stroke survivors relative to individuals who do not provide informal care to anyone (unexposed or reference group). It is the ratio of the incidence rates or proportions in the informal carer group to the reference groups derived from cohort studies that allows the calculation of the risk ratio (RR). The RR quantifies the magnitude of the strength of the association between informal care and depression¹¹⁹. If exposure to providing informal care to stroke survivors causes a change in the incidence of depression then there are the beginnings of an epidemiological basis for cause

and effect. Such information has important clinical and public health implications. However, there are additional criteria for example the temporal nature of the relationship or the scientific plausibility of the association, which need to be taken into consideration when attempting to determine whether an association is causal or not¹²⁶.

4.2.3 Types of epidemiological study

There are three main types of non-experimental epidemiologic study design which can be used to study the distribution and determinants of depression in a group of people who are exposed to providing informal care to stroke survivors: cohort studies, case-control studies and cross-sectional, including prevalence studies.

Cohort studies - all people in a source population who are free of the condition of interest (depression) at the outset and classified according to their exposure status (informal care-giving) and followed up over time to ascertain the incidence of depression (the condition of interest).

Case-control studies - cases of the condition of interest (depression) arising in a source population and a sample of the source population who are not depressed are classified according to their informal carer exposure history and other factors of interest.

Cross-sectional, including prevalence studies - exposure status and condition of interest status are ascertained at the same time, as of a particular time.

However, the validity and accuracy of any epidemiologic estimate is a product of the estimation process which includes; the study design, study conduct and data analysis⁴⁵. Threats to validity include confounding, selection bias and information bias.

4.2.4 Rationale for meta-analysis of epidemiological studies.

There are a number of reasons why meta-analysis is a suitable method for studying the distributions and determinants of the frequency of depression in

people who provide informal care to stroke survivors. First, meta-analysis is useful for combining and contrasting the results of different studies, particularly small studies with limited statistical power¹²⁷. The combined estimate (or summary effect measure) provides a more precise summary of the association with narrower confidence intervals compared to estimates from individual studies; it also provides a single, best summary estimate of the association between provision of informal care and adverse health outcomes. Second, meta-analysis is useful for identifying and estimating differences in study specific effects^{127;128}. Sources of systematic variation (heterogeneity) in study results include diversity of study methods and context. Finally, meta-analysis can be used to address questions not posed by the primary studies. Systematic reviews and meta-analysis use statistical methods to combine and summarise the results from multiple primary studies that address the same or a similar research question. These primary studies usually include individuals with specific characteristics and exposures which are clearly defined. A selection of these primary studies in which the population (or patient) or exposure characteristics differ can facilitate examination of the consistency of effect and if important, allow reasons for variability in the exposure effects to be investigated. Meta-analysis can help identify 'patterns among study results, sources of disagreement among those results and other interesting relationships that may come to light in the context of multiple studies'¹²⁹.

4.3 Background

Providing care to stroke survivors has been described as having a 'significant toll' on carers' health. There is a considerable body of evidence to support the link between providing unpaid care to a stroke survivor and depression in the informal carer. However, estimates of prevalence of depression in informal carers of stroke survivors vary widely in the literature in addition; the Glasgow Carers Cohort study (Chapter 3) failed to find a significant association between providing informal care to stroke survivors and depression; however this was a small single centre study with methodological limitations.

Therefore, the main question as to whether carers of stroke survivors are at higher risk of depression and if so, can these health effects be predicted remains largely unanswered thus far.

4.3.1 Description of the condition

Depression is the second most common mood disorder¹³⁰. The estimated prevalence of major depressive disorder (depression) by Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria in the United States of America was lifetime 16.2% (95% CI, 15.1-17.3) and 12 month 6.6% (95% CI, 5.9-7.3)¹³¹. The estimated point prevalence for a depressive episode by The International Classification of Diseases ((ICD 10), WHO, 1992) in the United Kingdom (UK) was 2.58% (95% CI, 2.23 - 2.92) among 16 to 74 year olds in 2000¹³².

Depression has a multifactorial aetiology and a number of risk factors have been identified these include; female gender, family history of depression, early adverse life events, stressful or negative life events, and lifetime history of any mental health problem are all associated with a significantly increased risk of depression¹³³.

4.3.1.1 Depressive disorder

Depressive disorder includes major depressive disorder and minor depressive disorder as defined by DSM-IV¹¹³ or depressive disorder defined by ICD 10²¹. According to DSM-IV¹¹³ for a diagnosis of major depressive disorder to be considered one of two core features must be present, either depressed mood or loss of pleasure and interest in activities and five other depressive symptoms from: feelings of hopelessness and helplessness, changes in appetite and weight, sleeping problems, decreased energy, feelings of agitation or of being slowed down, difficulties thinking, concentrating or making decisions, feelings of guilt and worthlessness, physical aches and pains, suicidal thoughts or attempts or plans and delusions or hallucinations. These symptoms must be present for over two weeks. The symptoms of minor depressive disorder are identical to the symptoms of a major depressive disorder episode, the difference being that fewer symptoms are needed to meet the diagnostic criteria (two out of nine

symptoms for major depressive disorder, one of the two being either depressed mood or loss of pleasure and interest in activities). Exclusions include a past episode of major depressive disorder or dysthymia.

4.3.1.2 Classification of depressive disorder

Categorical rating scales produce diagnostic judgements with regards to the presence or absence of major depressive disorder¹¹³ or depressive disorder¹³⁴ and adhere to current classification systems such as ICD 10²¹ or DSM-IV¹¹³. A categorical perspective to assessment of depressive disorder requires a structured clinical interview and a schedule or an interviewer administered examination. The structured clinical interview schedule requires the interviewer to count the number of criterion symptoms or conditions as present or absent.

Dimensional classification systems believe that depression is a region within a continuum which ranges from mild, self-limiting and present in the general population to severe, persistent and pathological¹³⁵. Dimensional rating scales produce information about an individual's comparative level of symptoms of depression or distress. These rating scales allow symptoms of distress to be placed on a continuum of severity based on symptom count, severity, frequency and duration. Dimensional rating scales can either be clinician administered or self-report. Most dimensional rating scales have been evaluated to determine optimal cut-point scores to identify those individuals who are likely to meet depression diagnostic criteria¹³³. The optimal cut-point is a value in an ordered sequence of values that is used to separate those individuals who are likely to meet mood disorder diagnostic criteria and those who are unlikely to be distressed. These optimal cut-points subsume several degrees of distress or endpoints including for example clinically significant or lesser degrees of distress marked by higher cut-points above the threshold cut-point. For example clinical cut point scores for the BDI-II¹¹⁶ are: 0 to13: minimal depression; 14 to 19: mild depression; 20 to 28: moderate depression; and 29 to 63: severe depression. Higher total scores indicate more severe depressive symptoms.

4.3.2 Description of the exposure

For the purpose of this research, the following assumptions have been made and definitions used. An individual is said to provide informal care if they interact with, with the intention of increasing the welfare of, an individual who needs supervision or assistance in illness or disability as a consequence of stroke and is living at a private address in the community. An individual who provides care is free-living; they are not defined by the presence of disease or ill health nor are they presenting for clinical care or under active health care. The individuals who provide care do not receive remuneration for the care they provide. Care is defined as the provision of what is necessary for the health, welfare, maintenance, or protection of another individual. 'Care' may include: help with personal care; basic health monitoring; medication management; emotional support; assistance with transportation; companionship; supervision in the home to avoid falls or household accidents; assistance with mobility; assistance with communication and household tasks (such as laundry, meals, light housekeeping, paying bills). This informal care is provided outside any formal context and therefore is not subject to any of the benefits of employment terms and conditions including regulations surrounding workplace, health, safety and welfare, working time limits, flexible working, sickness absence or paid time off for holidays. Care is considered to be a behavioural act and a factor that is exogenous to and not required for the normal functioning of the individual providing care and may alter health related states and events. Care is considered to be a chronic exposure in that the requirement to provide care is likely to continue over a prolonged period of time. The time of providing care is the time during which exposure accrues. The time at risk (or induction period) is the period of time between exposure to providing care to an individual who is sick, elderly or disabled and the onset of illness or adverse health outcomes in the individual providing informal care. The time at risk can extend beyond the end of the period of care provision for certain illness, health states and events. As noted in Chapter 3 there is currently no basis for hypothesizing a specific induction time between exposure to a specific amount of informal care and the subsequent effects, in this case onset of depression.

4.3.3 How the exposure might be a potential causal characteristic

The people who provide informal care are usually family, friends or neighbours. This infers an interpersonal and meaningful relationship. Therefore, there are several ways in which being in the position of providing informal care to another in illness, frailty or disability may result in depression. First, having a loved one or close friend have an acute illness event such as stroke can be considered to be a stressful life event. The consequences of this stressful life event may be a drastic, unplanned and crucially challenging change in for example interpersonal relationships, roles, financial status and life trajectory. Negative life events in personal relationships have been constantly linked with the onset of depression. Second, finding oneself in a position of providing what is necessary for the health, welfare, safety and health of another, may mean having to put aside concern for one's own interests, personal needs, goals, happiness, desires or well being. Finally, often the need to provide care is relentless, chronic, intense and crucially out of the carers control. Hard, constant graft does not necessarily bring about improvements or prevent deterioration in a care recipient's health condition, level of function or quality of life. While psychological motives for providing care may vary, it is possible to speculate about the size of the gains or rewards in comparison to the investment.

4.3.4 Why it is important to do this review

Uncertainties exist around the prevalence of depression in informal carers of stroke survivors with published estimates ranging from 34% to 52%¹³⁶. Moreover, the effect of an individual's exposure to informal care-giving on their risk of incident depression is unclear. Given that many stroke survivors rely on informal carers as their primary source of support, more reliable estimates on the effect providing informal care on the occurrence of depression and predictors of depression in people who provide care are needed to plan interventions; inform future clinical trials and shape public policy.

Therefore, the purpose of this study was to systematically review the published studies of people who provide care to stroke survivors and depression and to

critically appraise their methodological quality in order to combine comparable studies to answer several important questions:

Questions

- How frequent is depression in people who provide care to stroke survivors?
- Is providing informal care to stroke survivors associated with a higher incidence or prevalence of depression?
- Do definitions of the informal care-giving exposure influence the apparent incidence or prevalence of depression?
- Are care-giving factors or other socio-demographic factors (age, gender, marital status, ethnic group or socioeconomic status) associated with depression in people who provide care to stroke survivors?

Objectives

To obtain valid and precise estimates on the occurrence of depression in people who provide care to stroke survivors, to assess the association between exposure to providing informal care and depression and to identify factors associated with the development of depression in people who provide care to stroke survivors.

4.4 Criteria for considering studies for this review

4.4.1 Types of studies

Studies were included if they met the following criteria:

- The focus was on study participants as a provider of care to a stroke survivor living in the community that is, at a permanent address; therefore studies which focused on the effect on for example being married to a stroke patient on occurrence of depression were excluded.
- No restrictions on admissible participants (i.e., studies restricted to one sex or one age group of informal carers, one type of carer (e.g., live in carers, or spouses).
- No restrictions on type of stroke patient (e.g., patients with aphasia) and studies of mixed aetiology if the percentage of stroke patients was less than 80% were excluded.

- Depression was measured using standard criteria
- Types of epidemiologic study eligible include: cohort studies, case-control studies, including prevalent case-control studies and cross sectional studies, including prevalence studies.
- Must provide estimates of the occurrence of depression, in a binary format (i.e., depressed/ not depressed). Measures of frequency of depression include: incidence rate, incidence proportion and prevalence.

Incidence proportion was described as the number of new cases of depression divided by the whole population at risk over the period of the study.

Incidence rate was described as the incidence of new cases of depression divided by the person time over the period of study.

Prevalence was described as the proportion of people who have depression at a specific time.

Thereafter studies were evaluated against a bespoke checklist of ideal characteristics for a study of the effects of exposure to providing informal care to another in ill health or disability. Checklist items were based on the Newcastle Ottawa Scale¹³⁷, STROBE guidelines¹³⁸, guidelines for assessing prevalence studies¹³⁹, several key epidemiological textbooks¹⁴⁰⁻¹⁴², books on statistics¹⁴³ papers^{68;144;145} and clinical research text books¹⁴⁶. An overall study score was not developed, the focus instead was on study design, conduct or analysis that might affect the validity of conclusions.

General

- The study sample should be representative of the population of interest¹⁴³
- Source and methods of selection of participants clearly described¹⁴³
- Appropriate sampling strategy for study design^{139;143;146}
- Clearly defined eligibility criteria¹⁴³
- A clear, unambiguous definition of the informal care exposure¹⁴⁴
- An adequate case definition for depression¹³⁷
- An adequate exposure assessment strategy¹³⁷
- Standardised data collection methods¹³⁹

Prevalence of depression in people exposed to providing care to stroke survivors

- If cross sectional or prevalence study:
 - All persons in the population or a random sample of all such persons selected without regard to informal care or depression status or separately by informal carer exposure status¹³⁹.
 - recruit at least 80% of admissible participants¹³⁹
- If prospective cohort study:
 - Two types of cohort study design are ideal:
 - A single of people group of people (single cohort) who are free of the condition of interest, in this case, depression at the outset and are heterogeneous with regard to informal care exposure experience and are followed-up over a period of time. The aim is to compare the depression experience within the cohort and across subgroups defined by one or more exposures; or
 - Two or more groups of people who are free of depression at the outset and that differ according to the extent of their informal care exposure for example exposed to providing care to a stroke survivor or not exposed to providing care to anyone in illness of disability and are followed-up over a period of time. The aim is to capture and compare the depression experience (incidence proportions, incidence times, rates) in each of the study cohorts and to compare the measures of occurrence of depression.
 - All persons exposed or potentially exposed to providing care to stroke survivors in a population (for example from a population based register of stroke survivors) or random (either probability or consecutive) sample of all such persons selected^{137;143;146}.
 - Demonstration that the groups of people under study are free of the outcome of interest (depression) at start of study^{137;143;147}.
 - Inclusion rate of at least 80% of admissible participants followed-up of at least three months to allow depression to develop¹³⁷.
 - Follow-up 80% complete¹³⁷.
 - Clearly defined potential effect modifiers¹⁴⁸.

Incidence of depression in people who provide informal care to stroke survivors

- Prospective cohort study design. Types of cohort study as outlined above.
- All persons exposed or potentially exposed to providing care to stroke survivors in a population (for example from a population based register of stroke survivors) or random (either probability or consecutive) sample of all such persons selected^{137;143;146}.
- Demonstration that the groups of people under study are free of the outcome of interest (depression) at start of study^{137;143;147}.

- Inclusion rate of at least 80% of admissible subjects.
- Recruit participants over a sufficiently long period to account for any seasonal variations¹⁴⁶.
- Follow-up of at least three months to allow depression to develop.
- Follow-up 80% complete.
- Clearly defined potential effect modifiers¹³⁸.

Association of informal care exposure and depression

- If cross sectional or prevalence study:
 - All persons in the population or a random sample of all such persons selected without regard to informal care or depression status¹⁴⁷.
 - Recruitment rate of at least 80%.
- If prospective cohort study:
 - Prospective cohort study design, types of cohort study as outlined above¹⁴⁹.
 - All persons exposed or potentially exposed to providing care to stroke survivors in the population (for example from a population based register of stroke survivors and their informal carers recruited at time zero as a dyad) or a random (probability or consecutive) sample of all such persons selected^{137;143;146}.
 - Demonstration that the groups of people under study are free of the outcome of interest (depression) at start of study^{137;143;147}.
 - An appropriately chosen referent group¹³⁷.
 - Exposed and unexposed groups comparable on the basis of design or analysis¹³⁷.
 - Inclusion rate of at least 80% of admissible participants.
 - Recruit participants over a sufficiently long period to account for any seasonal variations¹⁴⁶.
 - Follow-up of at least three months to allow depression to develop¹³⁷.
 - Follow-up 80% complete¹³⁷.
 - Assessment of depression blinded to informal care exposure features of interest¹³⁷.
 - Clearly defined potential effect modifiers¹³⁸.
 - Clearly defined confounders¹³⁸.
- If case-control study:
 - All people in the source population who have developed the outcome of interest (depression) or a random sample of all people in the source population who have developed the outcome of interest (depression)^{137;143;146}.
 - Demonstration that the control group is free of the outcome of interest (depression)^{137;143;147}.
 - An appropriately chosen control group¹³⁴.
 - Comparability of cases and controls on the basis of design or analysis¹³⁴.
 - Non response rate similar in both case and control groups¹³⁴.

Factors associated with depression in people who are exposed to providing care

- Prospective cohort study design, types of cohort study as outlined above¹⁴⁹.
- All persons exposed or potentially exposed to providing care to stroke survivors in the population (for example from a population based register) or random (either probability or consecutive) sample of all such persons selected^{137;143;146}.
- Recruit participants at an identifiable, common and early point in their informal care exposure¹⁴⁹.
- Demonstration that the groups of people under study are free of the outcome of interest (depression) at start of study¹⁴⁹.
- Follow-up of at least three months to allow depression to develop¹³⁷.
- Follow-up 80% complete¹³⁷.
- Assessment of depression blinded to informal care exposure features of interest¹³⁷.
- Clearly defined confounders¹³⁸.

Table 4-1 Ideal design of different types of non experimental epidemiological studies (cross sectional or prevalence studies, cohort and case-control) which can generate data to answer different types of questions on: 1) the frequency of depression occurrence (incidence and prevalence) in informal carers of stroke survivors 2) the association between exposure to providing informal care and depression and 3) factors associated with depression in people who provide informal care.

4.4.2 Types of participants

Stroke survivor was defined as: Any living person who meets a clinical definition of stroke (World Health Organization (WHO) definition)¹⁵⁰.

Informal carer was defined as: any person of any age and gender who provides care to a stroke survivor outside any formal health, social or long term care context and without financial remuneration.

4.4.3 Types of exposure

There is no commonly agreed detailed definition for a current informal carer and there is no standard method for assessing and categorising the informal care exposure; therefore the study investigators' definition of the index condition for

a current informal carer, exposure groups/categories and method for measuring the level of exposure to informal care was accepted. This includes: the instrument used for exposure measurement (for example questionnaire, diaries, and structured interviews), the informal care exposure metric (for example number of hours care provided per week) and the definition for each informal care exposure category.

The study investigators reference conditions for unexposed would be used. For example, all those who fail to satisfy the current informal carer definition are classified as unexposed.

4.4.4 Types of outcome measure

For the purposes of this review depression is defined by e.g. a) a score above a threshold cut point on a clinician- or observer-related, or self-rated dimensional depression rating scale for example the Zung Depression Scale¹⁵¹ b) an interviewer-administered examination which adheres to a current classification system, for example DSM-IV¹¹³ c) a score above a threshold cut-point of a global-self-rated instrument with depression components for example the General Health Questionnaire (GHQ)¹⁵².

4.4.5 Search methods for the identification of studies

4.4.5.1 Electronic searches

The following electronic bibliographic databases were searched :

- MEDLINE (1950 to October 2010) (Appendix 12)
- EMBASE (1980 to October 2010) (Appendix 13)
- CINAHL (1982 to October 2010) (Appendix 14)
- AMED (Allied and Complementary Medicine) (1985 to October 2010)
- PsycINFO (1967 to October 2010)
- AARP (AgeLine) (1987 to December 2009)
- British Nursing Index and Archive (1985 to October 2010)
- Proquest Dissertations and Theses (1861 to October 2010)
- EMBASE Classic (1947 to 1973)

- HMIC Health Management and Information Consortium (1979 to October 2010)
- Social Work Abstracts (1968 to October 2010)
- Science Citation Index Expanded (SCI-Expanded)(ISI Web of Science 1900 to end October 2010)
- Social Sciences Citation Index (SSCI)(ISI Web of Science 1956 to October 2010), Arts & Humanities Citation Index (A&HCI)(ISI Web of Science 1975 to October 2010), Conference Proceedings Citation Index - Science (CPCI-S)(ISI Web of Science 1990 to October 2010), Conference Proceedings Citation Index - Social Sciences & Humanities (CPCI-SSH)(ISI Web of Science 1990 to October 2010).

The search strategies in conjunction with the Cochrane Stroke Group Trial Search Co-ordinator and adapted the MEDLINE strategy for the other databases.

4.4.5.2 Searching other resources

In an effort to identify further published, unpublished and ongoing studies:

(a) the following conference proceedings were searched:

European Stroke Conference (2006, 2007, 2008, 2009, 2010)

World Stroke Congress (2006, 2008, 2010)

UK Stroke Forum (2006, 2007, 2008, 2009, 2010)

(b) reference lists of relevant articles were searched

(c) authors and researchers in the field were contacted

Studies in all languages were searched for.

4.4.6 Data collection and analysis

4.4.6.1 Selection of studies

The titles and abstracts of all papers identified from the preliminary searches were reviewed by the principal review author (LL) to assess eligibility. Studies that did not meet the inclusion criteria were excluded at this stage. A paper copy of every potentially eligible study was obtained. Three review authors (LL,

TQ or CW) assessed all potentially eligible studies according to the pre-specified inclusion criteria. Disagreements were resolved by consensus.

4.4.6.2 Data abstraction and management

Published and unpublished data were sought for this review. Two review authors (LL, TQ) independently extracted data using a standardized data collection form. The features of interest included: attributes of each study's design for critical appraisal; details on the source of participants, method of assembly of cohorts, time period during which participants were identified and recruited, timing of assessments, depression rating scale used, data collection methods for example individual interview (face to face, telephone) or self-report or mixed, percentage females in the sample, average age of sample, definition of informal care exposure, definition of referent condition (if applicable), method of ascertainment of informal care exposure, selection of unexposed cohort, evidence that depression status was assessed at the start of the study, length of follow-up and the numbers of people above the threshold cut point for depression out of the total sample at first follow-up. Data were extracted on known risk factors for and correlates of depression⁴⁴¹ if their influence on the development of depression was investigated in the primary study. If known risk factors and correlates were evaluated for their influence on the development of depression in the primary study, then these factors were classified as 'assessed'. See table 4.4 Critical appraisal of studies included in this review. Data were also extracted on the relationship between additional socio-demographic variables, care-giving factors and other variables and depression. See Table 4-5 for full details of factors assessed in the primary studies. If necessary, further information was sought by correspondence with authors of the relevant studies. Discrepancies surrounding the eligibility of studies or data extraction were resolved through joint re-examination and discussion by reviewers and consensus. Several of the studies included in this review are described in more than one publication. Where study design was reported in multiple publications we used all the reports to inform our data extraction. Where additional analyses were performed, the analysis that provided the most complete information was used to avoid re-use of the same data.

4.4.6.3 Measures of occurrence of depression

This review is based on dichotomous (binary) data; therefore the outcome for every participant is only one of two possibilities; depression present or depression absent. For the purpose of this review measures of occurrence of depression include incidence proportion, incidence rate and prevalence.

Incidence proportion was described as the number of new cases of depression divided by the whole population at risk over the period of the study.

Incidence rate was described as the incidence of new cases of depression divided by the person time over the period of study.

Prevalence was described by dividing the number of cases of depression at a specified point in time by the sample size.

4.4.6.4 Measures of effect of exposure to providing informal care: prospective cohort studies

Risk difference (RD): (incidence proportion in the exposed cohort - incidence proportion in the unexposed cohort)¹²⁴.

If $RD > 0$, then the informal care exposure is associated with an increase in the probability of depression; if $RD < 0$, the informal care exposure is associated with a decreased probability of depression; if $RD = 0$, then exposure to informal care is not associated with depression¹¹⁹.

Risk ratio (RR): Is the ratio of the incidence proportions ((incidence of depression in exposed group/total number in exposed group)/ (incidence of depression in unexposed group/total number in unexposed group))¹²⁴.

If $RR = 1.0$, the informal care exposure and depression are not associated; if $RR > 1.0$, the informal care exposure is associated with an increase in the probability of depression; if $RR < 1.0$, the informal care exposure is associated with a decrease in the probability of depression¹¹⁹.

In addition to the estimates of measures of effect, 95% CIs will be used. 95% CIs define a range of values within which the 'true' value for the estimate of effect of the informal care exposure on the outcome of depression is likely to be found.

4.4.6.5 Measures of effect for cross sectional (prevalence studies)

Measures of effect for cross sectional (prevalence studies) included:

Risk ratio (RR): ((frequency of depression in exposed group/total number in exposed group)/ (frequency of depression in unexposed group/total number in unexposed group)). Explanation of RR as above.

4.4.6.6 Measures of effect for case-control studies

Exposure odds ratio (OR): ((frequency of depression in the exposed group/frequency of no depression in exposed group)/ (frequency of depression in unexposed group/ frequency of no depression in unexposed group) ¹⁵⁴.

Calculation of exposure OR

	Exposed	Not exposed	Total
Depressed +	a	b	a+b
Depressed -	c	d	c+d
Totals	a+c	b+d	a+b+c+d

Exposure OR = ((a/c)/ (b/d)) or ad/bc

4.4.6.7 Measures of association between depression in informal carers and predictor variables

Where depression is presented as a binary outcome (that is depression present or absent), crude or adjusted odds ratios will be used as a measure of association together with the 95% CI and P value if a test of significance is performed.

Where depression is presented as a continuous dependent variable, correlation coefficients (r) (and their 95% CI and level of significance) and regression coefficients (β) will be used as measures of strength of association along with their 95% CIs and hypothesis tests¹¹¹.

4.4.7 Dealing with missing data

The primary aim of this review was to obtain standardised data through collaboration with the original study investigators. Where data were missing from a published report the primary investigators were contacted in an attempt to get this information.

4.4.8 Assessment of heterogeneity

Heterogeneity was assessed by visually examining forest plots and by performing the χ^2 test using a p-value of less than 0.1 to indicate heterogeneity. A p-value of less than 0.1 was used rather than the conventional cut point of 0.05 because of the low power of this test¹⁵⁵. The effect of heterogeneity was quantified using the I^2 statistic including its 95% CI¹⁵⁵. The I^2 statistic expresses the proportion of variation in estimates that is due to between study heterogeneity rather than sampling error or chance¹⁵⁵. The value of the I^2 statistic ranges from 0% to 100% with 0% representing no observed heterogeneity to larger number representing increasing heterogeneity¹⁵⁵. An I^2 value greater than 50% was considered substantial inconsistency¹²⁷.

4.4.9 Assessment of reporting biases

Reporting biases were assessed using a funnel plot¹⁵⁶.

4.4.10 Data synthesis

4.4.10.1 Prevalence and meta-analysis of prevalence

The pooled estimate of prevalence of depression was calculated by combining the data from all studies that reported prevalence at the first phase of cohort follow-up. The standard error of the proportion was calculated using $(SE = \sqrt{(p)(1-p) / n})$ ¹⁵⁷. An inverse variance approach with a fixed effects model was used to calculate the pooled prevalence estimate and 95% confidence interval [95% CI]¹⁵⁵.

4.4.10.2 Incidence and meta-analysis of incidence

The plan was to pool the estimate of the incidence of confirmed symptoms of depression by combining the data from all the studies that reported either incidence rate or incidence proportion. An inverse variance approach with a fixed effects model to calculate the pooled incidence estimate and 95% confidence interval [95% CI]¹⁵⁵ was planned. A sensitivity analysis to test the sensitivity of the results to the choice of model was planned.

4.4.10.3 Meta-analysis of difference measures

The aim was to calculate the incidence of confirmed symptoms of depression during the follow-up period and calculate the risk difference (excess risk due to exposure) with a 95% CI. The aim was to pool the risk differences using Mantel-Haenszel methods¹²⁷. The plan was to use a fixed effects analysis unless there was evidence of heterogeneity ($p \leq 0.1$) in which case a random effects meta-analysis would be used¹²⁷.

4.4.10.4 Meta-analysis of Unadjusted Effect Estimates

The aim was to report adjusted risk ratios (RR) (crude estimates that are corrected for the effects of confounding factors) if available otherwise, to calculate unadjusted RRs (crude estimates that are not corrected for the effects of confounding factors) using incidence proportions.

The plan was to pool unadjusted effect estimates using Mantel Haenszel methods¹²⁷. The basic data for the unadjusted analyses consists of a series of two by two tables, one for each individual study. The two by two tables are created by considering two dichotomous variables: the exposure variable is 'provides informal care to a stroke survivor' or 'does not provide informal care to a stroke survivor' and the disease variable is the presence or absence of depression that is scoring above or below the recommended clinical cut-point. We planned to extract the data for the two by two tables from the information provided by the authors of the individual studies.

4.4.10.5 Meta-analysis of Adjusted Effect Estimates

For the analysis of the adjusted data, the plan was to extract the RR with 95% CI that had been adjusted for potential confounders during the design phase (for example matching) or analytic methods during the analysis phase or both. The basic data needed from each study for a meta-analysis of adjusted effects is an adjusted RR and an estimate of its standard error, which can be obtained indirectly from a confidence interval if reported.

For crude and adjusted meta-analysis a fixed effects model with Mantel-Haenszel methods was planned to combine studies when I^2 was $\leq 50\%$. Otherwise, a random effects model according to the DerSimonian Laird¹⁵⁸ method was planned¹⁵⁵.

4.4.11 Identification of factors associated with depression

To identify the factors associated with depression in people who provide care to stroke survivors the plan was to calculate summary odds ratios for sociodemographic factors, known risk factors for depression and care-giving characteristics with a fixed effects analysis unless there was evidence of heterogeneity ($p \leq 0.1$) in which case a random effects model would be used.

In all cases, the aim was to summarise the data statistically, as above, if data were available, sufficiently similar and of sufficient quality.

4.4.12 Stratified analysis and investigation of heterogeneity

The plan was to investigate heterogeneity among studies by using a process of stratification analysis¹²⁰ to determine the sources of heterogeneity. The selection of stratification variables is dependent on the individual subject matter under investigation and on knowledge of the studies. Moreover, it is necessary to have all the information available to allow the each study to be classified by the stratification variable of interest. The stratification variables of interest in this study included age, gender, country or region of origin, between study protocol differences including study eligibility criteria, methods of data collection for example mail-in questionnaire or face to face interview,

depression diagnostic criteria, average duration of follow-up. However, due to a limited number of studies per covariate and limited available information, this was not possible¹²⁷.

Revman 5.1 software for all statistical analyses¹⁵⁹.

4.5 Results

4.5.1 Description of studies

4.5.1.1 Results of the search

1623 titles and abstracts were screened and 120 were selected for further detailed examination (Figure 4.1). Nineteen studies^{62;160-177} were identified for further assessment. One¹⁷⁷ of the 19 studies is still awaiting assessment. Of the remaining 18 studies, eight studies provided all the required data. The authors of the remaining ten papers^{161;163-165;167;168;171;172;174;176} papers were contacted.

4.5.1.2 Included studies

12 studies were single cohort design^{160;161;163 62;167;168;170-174;176} and six studies used a cross sectional study design. The included studies presented data on the proportions of people (prevalence) who met the criteria for depression at specific times over the follow-up period (cohort studies) or at the time of assessment (cross sectional studies). No cohort study presented data on new cases of depression per unit of person-time (incidence rate) or the proportion of participants who developed new depression over the period of the study (incidence proportion). Mean age of participants ranged from 41.2 years¹⁶⁶ to 66.9 years¹⁶³; between 62%¹⁶⁸ and 91%¹⁷⁴ of participants were women. For cohort studies, the length of time between baseline and first follow-up ranged from four weeks to six months. For cross sectional studies, the time from stroke onset to assessment ranged from three or more months of care-giving experience¹⁶⁶ to three years post stroke¹⁶³. The Centre for Epidemiologic Depression Scale was the most frequently used rating scale^{162;167;169;170;173;176} followed by the Hospital Anxiety and Depression Scale^{62;165;166;168;175}.

For full details of the included studies see table 4-2: Characteristics of included studies.

4.5.1.3 Excluded studies

For details of excluded studies please see table 4-3: Characteristics of excluded studies.

4.5.2 Quality of the included studies

4.5.2.1.1 Clear definition of the informal carer exposure

One study¹⁶⁴ provided a clear, unambiguous and measureable definition of the informal carer exposure (Table 4-4).

4.5.2.1.2 Appropriate ascertainment of informal care exposure

One study¹⁶⁰ used providing at least two activities from the Oberst Caregiving Scale (OCBS)¹⁷⁸ as criteria for determining whether potential participants were exposed to providing care or not. Participants who were providing fewer than two activities on the OCBS were excluded from the study. One study¹⁶² used providing assistance with one activity from the Carer assistance scale as a measure of exposure to providing informal care. No other studies reported using other instruments for informal care-giver exposure assessment for example structured interviews or questionnaires. No study reported measuring informal carer status at first follow-up assessment (Table 4-4).

4.5.2.1.3 Clear definition of participants informal care exposure history.

One study¹⁷⁴ recruited people who were new to providing care to stroke survivors. No other study provided information of previous care-giving exposure history (Table 4-4).

4.5.2.1.4 Depression free at recruitment

No study reported recruiting participants who were free of depression at the start of the study (Table 4-4).

4.5.2.1.5 Recruit participants at an identifiable, common and early point in their informal care exposure

Only one study¹⁷⁴ reported recruiting participants who had no previous experience of providing care (Table 4-4).

4.5.2.1.6 Generalizability of participants

Only six studies^{62;161;164;166;168;173} had reasonable generalizability. The main reasons for poor generalizability were convenience sample^{160;162;165;167;171;174-176}, less than 80% admissible subjects recruited or responded^{162;169;170;175;176} or percentage of admissible subjects not known^{160;171;172;174}; and less than 80% response or follow-up^{163;170;172} (Table 4-4).

4.5.2.1.7 Blinded assessment of outcome

Two studies^{165;176} reported mailing the follow-up questionnaires including depression rating scale for completion and return. One study reported self-completion of the depression rating scale whilst waiting for an appointment¹⁷⁴. With regards to the other 16 studies, it is not clear from the published reports as to whether the outcome assessor was blind to the purpose of the study or the care-giving status of the participant (Table 4-4).

4.5.2.1.8 Risk factors for and correlates of depression clearly defined.

One study explored depression occurrence in different subgroups by care-giver care recipient relationship¹⁶¹ however, the data was presented as a means and standard deviations not estimates of prevalence. Five studies explored the relationship between depression with carer age^{62;163;170;173;174}, three with gender^{62; 170;174}, one with employment¹⁷⁰, one with income¹⁷³ and one with ethnic group¹⁶⁷. Other factors explored in the studies include: carer health, carer skills and attributes, carer personal and care-giving factors including stroke survivor characteristics. For full details of the factors explored see Table 4-5.

4.5.2.1.9 Ideal design of studies of prevalence

16 studies provided data from which prevalence estimates could be either extracted or calculated using data from primary investigators. Of these 16 studies, four studies^{161;166;168;173} met most of the desired criteria. The other twelve studies provided data on prevalence, but these studies met few of the desired criteria. With these limitations in mind, the evidence from these

studies has been used to address the important questions about prevalence of depression in people who provide care to stroke survivors.

4.5.2.1.10 *Ideal design of studies of association between informal care and depression in people who provide care to stroke survivors*

No studies met the inclusion criteria for studies of association between informal care and depression.

4.5.2.1.11 *Ideal design of studies examining factors associated with depression in people who provide care to stroke survivors*

Seven studies^{62;161;163;167;170;173;174} explored the association between a number of factors of interest and depression. For details of factors explored see table 4-5: Influence of demographic, care-giver, care-giving and stroke survivor factors on prevalence on depression in people who provide care to stroke survivors.

No study met our ideal inclusion criteria.

4.5.2.2 *Frequency of depression in people who provide care to stroke survivors*

4.5.2.2.1 *Prevalence of depression*

The prevalence proportions ranged from 13% to 50%. The pooled prevalence estimate calculated using the inverse variance method using a random effects model was 28% (95% CI 23%, 33%) ($p < 0.001$; I² 81%), aspects of study design may account for some of the heterogeneity among these studies. Restriction of meta-analysis to studies with ideal study design the pooled prevalence estimate calculated using the inverse variance method using a fixed effects model was 30% (95% CI 25%, 34%) ($p < 0.001$; I² 0%), however there is clearly consistency between the full and restricted analysis results. See figure 4-2.

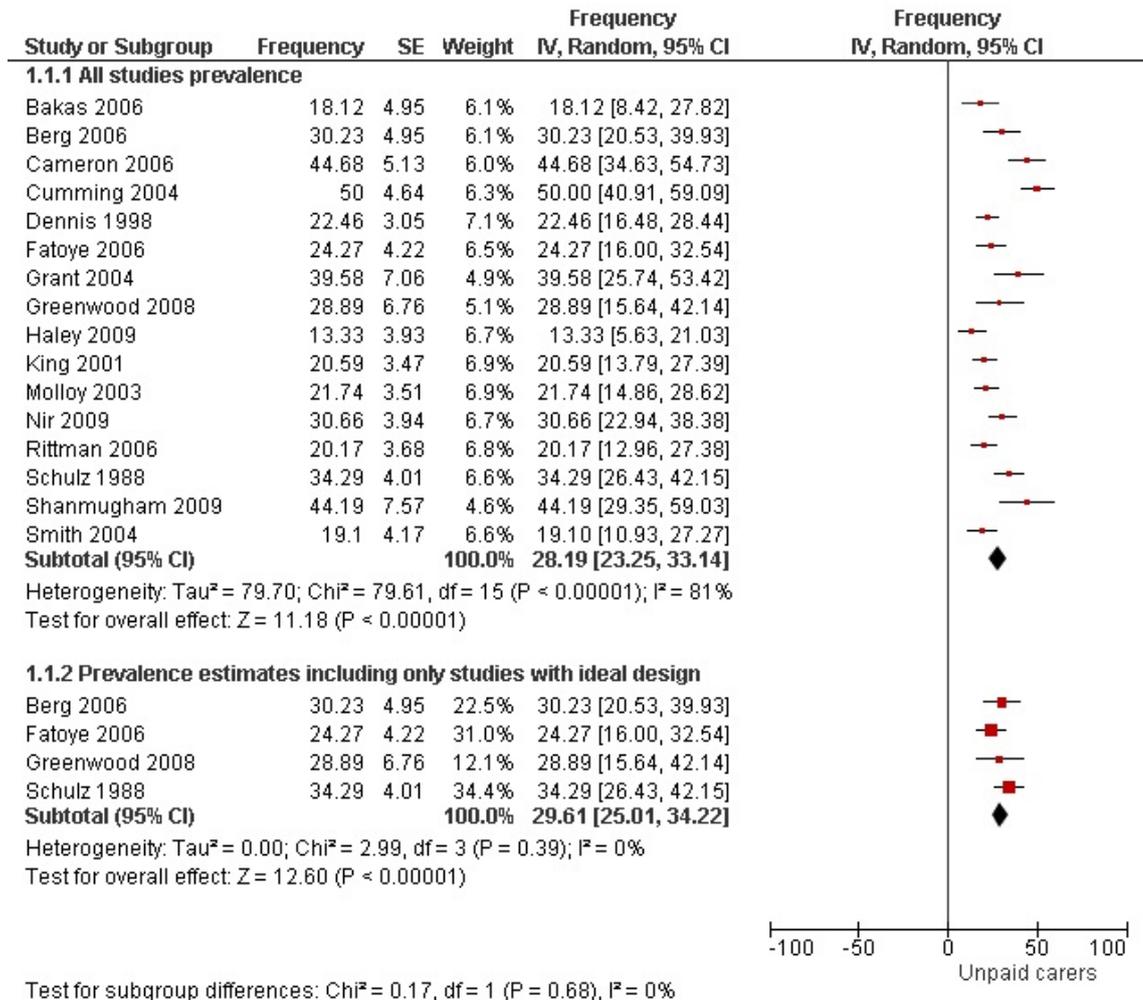


Figure 4-2 Forest plots of estimates of prevalence of depression. Forest plot 1.1.1 is the estimates of prevalence from all included studies. Forest plot 1.1.2 is the prevalence estimates when analysis is restricted to studies with ideal characteristics.

Forest plot produced using the generic inverse variance method in Revman 5.1¹⁵⁹. Illustrated is the summary data (point estimates (squares) and confidence intervals (horizontal lines through squares) for each study and a meta-analysis for each subgroup (full (1.1.1) and restricted (1.1.2) analysis) using a random effects model illustrated by a diamond. Also presented are the weights given to each study and heterogeneity statistics (among study variance Tau², χ^2 test and I² statistic).

4.5.2.3 Reporting biases

The funnel plot suggests that there may be some studies missing. However, it is difficult to judge with so few studies. See figure 4-3.

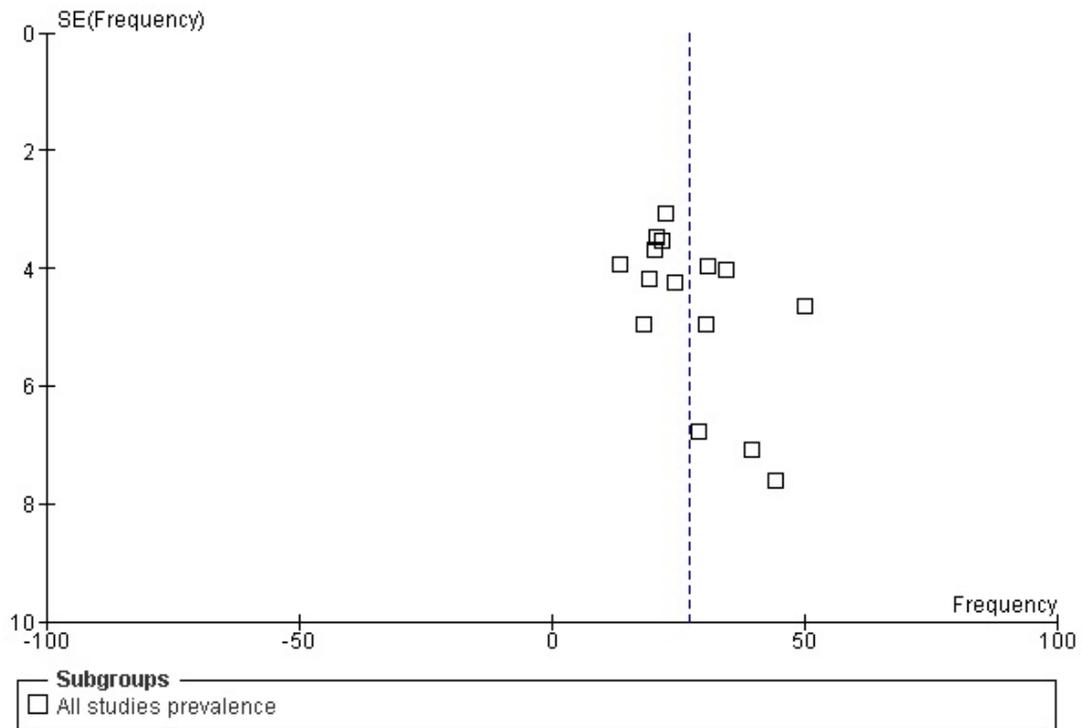


Figure 4-3. Funnel plot of the estimates of prevalence of depression from individual studies against the standard error of the prevalence estimate. The horizontal axis represents the estimates of prevalence of depression. The vertical axis represents the standard error of the prevalence estimate.

4.5.2.3.1 *Incidence of depression*

No cohort studies were found which met the inclusion criteria and aimed to measure the incidence (incidence rate or proportion) of depression either in a single cohort of informal carer or in two or more cohorts, one of which was an exposed informal care-giving cohort and the other is unexposed, or reference cohort.

4.5.2.3.2 *Is providing informal care to stroke survivors associated with a higher incidence or prevalence of depression?*

No studies were found which met the inclusion criteria.

4.5.2.4 **Do definitions of informal care-giving exposure influence the apparent incidence and prevalence of depression?**

Lack of clear, unambiguous definitions of the informal care exposure made it difficult to assess the impact of the definition of informal care on the prevalence of depression in people who are assessed to provide care.

4.5.2.5 Examination of care-giving and socio-demographic factors (age, gender, marital status, ethnic group or socioeconomic status) associated with depression in people who provide care to stroke survivors.

Several studies^{62;161;170;173;174} have repeatedly measured multiple factors of interest and depression scores over time and have correlated the two variables without taking the time trends into account. One study¹⁶⁷ reports the association between depression and four variables including ethnic group assessed one to two days prior to the stroke survivor being discharged from hospital. No data additional data are presented on the association between two or more variables at any point of community follow-up.

One study¹⁶³ found that the odds of being depressed was lower OR = 0.51(95% CI 0.32, 0.81, p = 0.004) in the group which had higher social support. The study also found that the odds of depression were greater for people who provided care to stroke survivors who had high irritability, depression and anxiety scores (OR = 1.09 (95% CI 1.02, 1.16, p = 0.007).

One study⁶² presented a cross sectional multi-level modelling analysis for two time points, one at two weeks (time 1) and one at eight weeks (time 2) post discharge from hospital. After controlling for carer age, gender and relationship to patient the overall model for depression was found to be statistically significant at time 1 ((adjusted R² = .13, F (6,118) = 4.04, P< .05) and time 2((R² change = .15, F (6,119) = 4.63, P< .05). High demand and low control were associated with higher depression at time 1 (β = .20, p<0.5) and β = -.27 (p<.01) respectively. Low control was associated with higher depression at time 2 (β = -.33 (p<.01). Data on the standard error or confidence interval was not presented for either result. This analysis was based on a sub-group of 138 carer/patient dyads (out of 172 carers recruited) for whom all the data were available.

It was not possible to extract data on the prevalence of depression by subgroups of risk factors such as age and gender from any of the remaining studies.

4.6 Discussion

4.6.1 Summary of the main results

These results indicate a relatively high prevalence of depression at around one in three care-givers; however there were insufficient published data to determine the excess risk associated with exposure or the association between exposure to providing informal care to stroke survivors. Data on associates of depression in people who provide care to stroke survivors comes from one small study assessing the influence of potential risk factors at three years post stroke onset.

4.6.2 Overall completeness and applicability of evidence

There are four main limitations. First, the index condition for an informal carer is not reported in precise detail in any of the studies. For example, a detailed definition of the index condition for a current informal carer might account for the frequency of informal care activities (for example the number of care related activities performed in a day), the number of hours care provided per week, the duration of informal care (for example months) and the age at which informal care began. The identification of those who classify themselves as an informal carer based on relatively loose definitions (for example 'A person who lives with the patient and is most closely involved in taking care of him/her at home') is not the equivalent to the identification of those who actually provide informal care. The definition of informal carer is crucial when considering the effects of informal care (informal carer versus not carer) on the incidence or prevalence of depression. For the words 'informal carer' to have substance it is important to be able to picture the informal carers, the incidence or prevalence of depression, and what the incidence or prevalence would have been if we replaced the informal carers with people who are not informal carers. This highlights the vague meaning of informal carer and the importance of defining the index (informal carer) and reference (not carer) conditions in sufficiently precise detail. A substantial definition of informal carer is essential to determine who satisfies the current informal carer definition as exposed. Similarly, there needs to be a substantial definition of the absence of the

informal care exposure, the reference condition. Detailed definitions will assist with the interpretation and application of the results.

Second, is the assumption that the informal care exposure is a *permanent and easily identifiable condition*⁴³⁷, making the task of assigning participants to providing informal care (exposed) and not providing informal care (not exposed) groups a simple activity. This point is demonstrated in the assembly of study cohorts based on identifying and classifying individuals as to their notional informal exposure status at the start of follow-up and subsequent treatment as a fixed cohort, that is, no anticipated movement out of the exposure groups. The reality, as demonstrated by the GCCS (Chapter 3), is quite different. People who provide informal care today may not provide informal care tomorrow and vice versa. Therefore, ideally the definition of the informal care exposure should be attached to time as the informal care exposure can vary over time. The fixed cohort approach does not account for the fact that the informal care exposure can change with time.

Third, is the assumption that the informal care exposure is continuous. Evidence against this assumption is provided by the GCCS (Chapter 3). Results from the GCCS suggest that people who are exposed to providing informal care can move through and between various levels of exposure. Figure 3.11 illustrates the need to classify the experience of a single participant in different exposure categories (number of hours care per week) at different time points and highlights the numerous potential exposure sequences.

Fourth, the effects of the informal care exposure may happen immediately, occur gradually, or start after a delay. It is also possible that disease frequency measures will vary with informal care exposure. Studies do not take into account the need to classify the experience of one informal care exposure in different exposure categories at different times.

Furthermore, without a clear, unambiguous and measurable definition of current informal carer it is impossible to disaggregate chronically depressed mood and unpaid care role-related stresses from the potential effects of stressful life events such as the sudden onset of stroke in a close relative or loved one and moreover, the potential enduring stressful consequences of such an event which

may mediate the depression for example loss of employment and attendant loss of income¹⁸, feelings of loss and grief ‘for the way that their life and that of the person they care for, has changed’¹⁴².

4.6.3 Quality of the evidence

The aim of this review was to produce valid and precise epidemiological estimates of the frequency of depression in people who provide care to stroke survivors and the effect of the informal care exposure on the occurrence of depression and to identify associates of depression.

The estimate of prevalence this review comes from 16 studies from seven countries carried out over the previous 25 years. The prevalence estimates is based on data from a total of 1848 participants at the first phase of follow-up in cohort studies which ranged from eight weeks to six months after recruitment or from cross sectional studies carried out on average one year after stroke onset. A number of different rating scales were used to assess depression. It is difficult to draw robust conclusions on the proportion of people exposed to providing informal care who have depression as there is a lack of a clear, unambiguous definition of the informal care exposure across all the studies. Furthermore, the procedures used by some studies to select participants and high attrition rates (cohort studies) or lower response rates (cross sectional studies) introduce the possibility of selection bias. However, in an attempt to correct for possible selection bias in the original studies a more strict inclusion criteria was applied, that is studies that had pre-determined ideal study design characteristics only were included, and the data were re-analysed giving slightly higher estimates of prevalence of depression, although there is considerable overlap of the confidence intervals, with no heterogeneity.

In addition, it is possible that the magnitude of the depression may vary for example by stratum for example by demographic characteristics including age, gender, ethnic group, marital status or socioeconomic status all known risk factors for depression. However lack of available data made it difficult to examine stratum specific estimates, therefore confounding factors might also account for some studies’ observations (for example the estimates of prevalence may be due to the recruitment of females, there is a well known association

between being female and being an informal carer and females are at increased risk for depression, thereby raising the prevalence of depression).

In addition to bias and confounding, small sample sizes make random error a further explanation for the findings.

4.6.4 Potential biases in the review process

The funnel plot would suggest that a few studies are missing from the analysis. Every effort has been made to identify all the studies that meet the review inclusion criteria. All studies were sought regardless of language of publication. In the event that more data was required, all of the original study authors bar one were contacted successfully.

4.6.5 Agreements and disagreements with other studies or reviews

The strengths of this review are its systematic and comprehensive nature, using a predefined protocol, including only those studies with generalizable populations. This approach was not taken by previous narrative reviews¹ and may account for the lower estimates of prevalence rates of depression found in this review.

The National Comorbidity Survey Replication (NCS-R MDD)¹³¹ and the UK ICD depressive episode prevalence estimates¹³² are markedly lower than the prevalence estimates for informal carers of stroke survivors. There are several reasons why this may be the case.

Both the NCS-R MDD¹³¹ and the UK Psychiatric morbidity among adults living in private households 2000 Survey (PMAALPH)¹³² used categorically based classification systems and yield information on prevalence of major depressive disorder or depressive episode based on the number of people who meet the diagnostic criteria for depressive disorder. In contrast, the studies included in this review use self-report dimensional rating scales to yield information on depressive symptom count, severity, frequency and duration. For the purposes of this review published cut-points¹³³ have been used to estimate the number of

participants who are who are likely to meet diagnostic criteria for depression. Therefore, the prevalence estimated in this review is the proportion of the study population, who may have clinically significant symptoms of depression at the specified time of assessment and not the number of cases. Therefore, the sizeable difference in prevalence may be due to the differing case definitions and the diagnostic procedures or assessment tools being used. Community studies have found that some depressive symptoms such as sadness or dysphoria, thoughts of death, changes in sleeping pattern or appetite are relatively common with prevalence proportions ranging from 20% to 30% in the general population^{281;282}. Moreover, the presence of a few depressive symptoms, too few to meet the diagnostic criteria for major depressive disorder can be found in 9% to 24% of the population depending on the assessment tool used^{283;284}. In the primary care setting, the prevalence of subclinical forms of depressive disorder (that is does not meet the criteria for depression) is more common than major depressive disorder with prevalence estimates ranging from 27% to 41%²⁸⁵⁻²⁸⁸. Therefore, the estimate of prevalence of depression found in this review is similar to the prevalence of sub threshold forms of depression found in community studies and in the general population.

4.7 Conclusions

This review lends cautious support to the hypothesis that the informal carer role (and related stresses) may be associated with depressed mood. It can be concluded that symptoms of depression are common in informal carers but it remains unclear whether providing informal care to a stroke survivor is a cause of depression.

4.8 Implications for practice

Clinicians should be aware that in addition to the physical and socioeconomic demands of providing care, as many as one in three carers are likely to experience a significant burden of depressive symptoms. This should be taken into consideration when stroke survivors attend outpatient and rehabilitation visits with their informal carer.

4.9 Implications for research

Greater rigour in the definitions of informal care used in future studies is urged. Definitions should include the required duration, frequency and intensity of care provided in order to be termed a carer. Due to the changing nature of required care over the course of a disorder, researchers should re-assess the level of care provided at each assessment. Controlled studies are also needed which include a control group that is not exposed to care giving. In addition, the rigorous and explicit methods used in this review may also be valuable or indeed necessary in the wider context of systematic reviews and meta-analysis of the relationship between exposure and disease.

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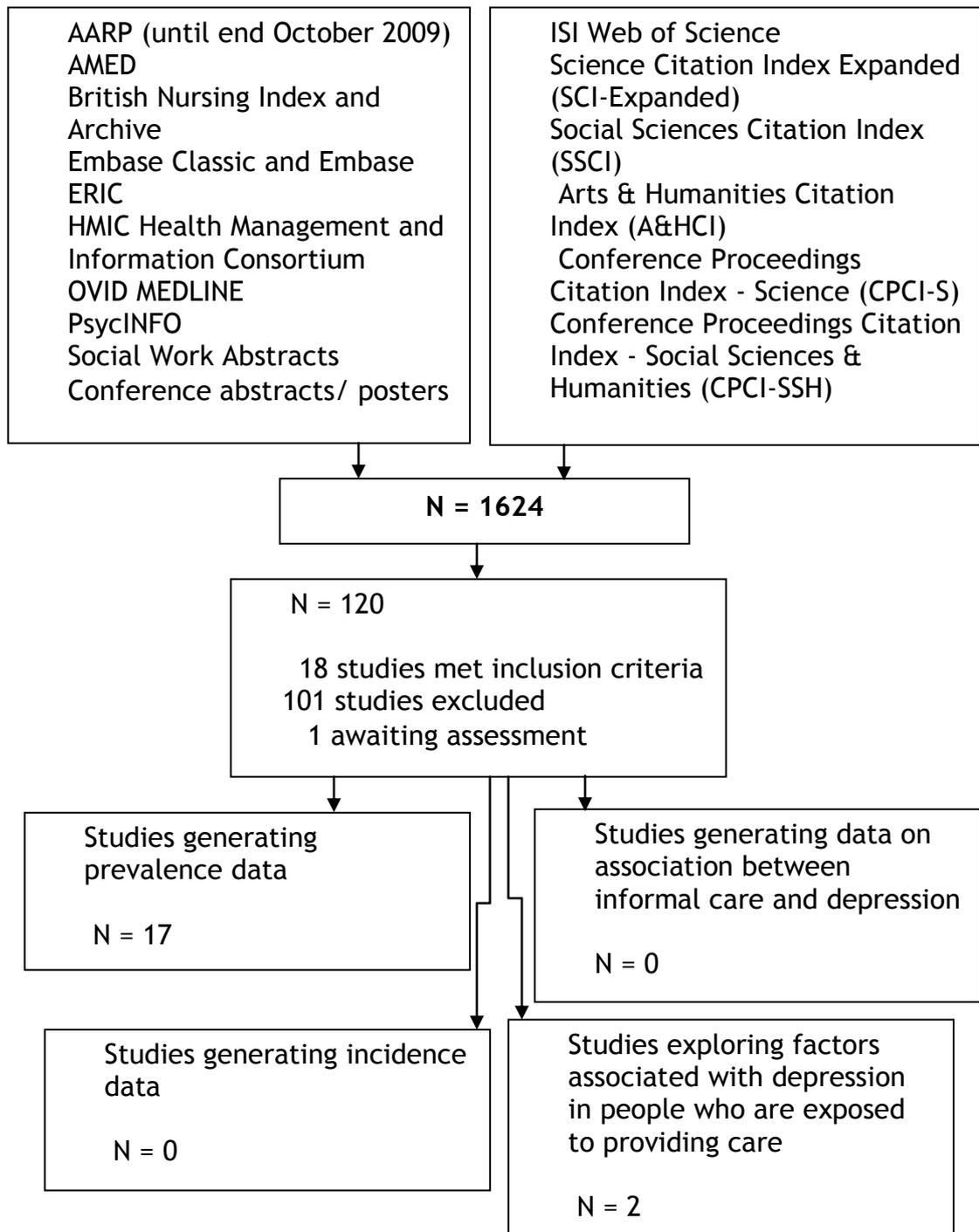


Figure 4-1 Flowchart of selection of studies for inclusion in the systematic review and meta-analysis.

Table 4-2 Characteristics of included studies

Bakas et al., 2006 ¹⁶⁰		
Participant identification and recruitment	Country & Study design	USA, cohort study
	Source of participants	Carers recruited from hospitals and clinics.
	Assembly of cohort of carers or sample for cross sectional study	<p>Sampling design: Convenience sample of carers recruited from hospital and clinics.</p> <p>Definition of the informal care exposure: None</p> <p>Criteria for determining informal carer exposure status: Two activities performed from the Oberst Caregiving Burden Scale (OBCS).</p> <p>Eligibility criteria: unpaid family carer or significant other of a stroke survivor living at home within one month after stroke who could read and write and performed a minimum of two care-giving tasks on the OBCS.</p> <p>Selection process: not stated</p>
	Time period	Not stated
Methods	Timing of assessment	1 month and 4 months after stroke
	Rating scale and clinical cut point for detecting depression	PHQ-9 (score ≥ 10)
	Assessment methods	Questionnaire in clinical setting or by telephone
Results	Total number admissible	Unclear
	Total number enrolled	159
	Number assessed/ response	159 at one month 149 at 4 months
	N(%) females of total sample	125 (78.6%)
	Mean age	mean 51.7 (SD 13.7: range 21 to 78 years)

	(SD)	
	Proportion of participants scoring above the cut point measure of depression	1 month 29/159 (18%) 4 months 27/149 (18%)*
Berg et al., 2006 ¹⁶¹		
Participant identification and recruitment	Country & Study design	Finland, cohort study
	Source of participants	A consecutive sample of first ever stroke patients aged ≤ 70 , admitted to the department of neurology, Helsinki University Central Hospital, and their carers.
	Assembly of cohort of carers or sample for cross sectional study	Sampling design: Convenience sample of carers of 100 stroke patients aged > 70 with first ischaemic stroke. Definition of the informal care exposure: Not stated Criteria for determining informal carer exposure status: The person providing closest contact with the stroke patient. Eligibility criteria: Not stated Selection process: unclear
	Time period	April 1990 to January 1993.
Methods	Timing of assessment	Acute phase mean 26.6 days after acute stroke, 6 months and 18 months.
	Rating scale and clinical cut point for detecting depression	BDI 21(score ≥ 10)
	Assessment methods	Interview/self-report
Results	Total number admissible	98
	Total number enrolled	98
	Number assessed/ response	At mean 26.6 days = 95 6 months = 86* 18 months = 79
	N(%) females of total	Not provided

	sample	
	Mean age (SD)	Not provided
	Proportion of participants scoring above the cut point measure of depression	Baseline 31/98(33%) 6 months 26/86(30%)* 18 months 24/79(30%)
Cameron et al., 2006¹⁶²		
Participant identification and recruitment	Country & Study design	Canada, cross sectional study
	Source of participants	Participants identified from rehabilitation outpatient clinic, tertiary care facility outpatient clinic, and community care organizations.
	Assembly of cohort of carers or sample for cross sectional study	Sampling design: convenience sample Definition of the informal care exposure: The person primarily responsible for providing and/or co-ordinating care in the home for the stroke survivor. Criteria for determining informal carer exposure status: one activity of the Caregiver Assistance Scale. Eligibility criteria: provided assistance with one activity on the Caregiver Assistance Scale (CAS) Selection process: Research assistant asked if the potential participant provided assistance with any activity on the CAS. If they provided help with one activity they were asked if they would like to participate in the study.
	Time period	Between August 2000 and June 2001.
Methods	Timing of assessment	mean 21.5 (\pm 5.82) months after stroke onset
	Rating scale and clinical cut point for detecting depression	CES-D-20 (score \geq 16)
	Assessment methods	Face to face interview or mailed survey.
Results	Total number admissible	142
	Total number enrolled	-

	Number assessed/ response	94 (66%)
	N(%) females of total sample	74 (78.7%)
	Mean age (SD)	mean 60.8 (\pm 15.41 years)
	Proportion of participants scoring above the cut point measure of depression	42/94
Cumming et al., 2004¹⁶³		
Participant identification and recruitment	Country & Study design	Australia, cohort study
	Source of participants	A consecutive sample of stroke patients aged \leq 18 admitted to one of 12 public hospitals in metropolitan Melbourne (Victoria, Australia) and their carers.
	Assembly of cohort of carers or sample for cross sectional study	Sampling design: A consecutive sample of stroke patients and their care-givers. Definition of the informal care exposure: not stated Criteria for determining informal carer exposure status: unclear Eligibility criteria: unclear The process of identification of carer: unclear. Selection process: unclear
	Time period	September 1998 and 1 October 1999
Methods	Timing of assessment	3 years after stroke onset
	Rating scale and clinical cut point for detecting depression	Irritability, depression, and anxiety scale (IDA)(score 4-15)
	Assessment methods	Telephone or face to face interview
Results	Total number admissible	468
	Total number	416

	enrolled	
	Number assessed/ response	At 8 weeks = 416 At 6 months 222 At 3 years = At 3 = 116
	N(%) females of total sample	At 3 years 71%
	Mean age (SD)	At 3 years, mean 66.9 (SD13.3)
	Proportion of participants scoring above the cut point measure of depression	8 weeks - depression data not collected 6 months- depression data not collected 3 years - 58/116
Das et al., 2010¹⁶⁴		
Participant identification and recruitment	Country & Study design	India, cross sectional study
	Source of participants	Population of Kolkata city, India, using a stratified random sampling design. Study period: November 2003 - April 2008.
	Assembly of cohort of carers or sample for cross sectional study	Sampling design: Probability sample stratified random sampling design. Definition of the informal care exposure: the unpaid person closely involved in physical (feeding, bathing, toileting, walking) and emotional care (empathetic listening, encouragement and motivation to adhere to treatment). Criteria for determining informal carer exposure status: unclear Eligibility criteria: Stroke survivor must require regular carer help as assessed by abnormal scores on Barthel Index, Bengali version of the mental status examination, for cognitive screening, the Geriatric Depression Scale and the Everyday abilities scale for India. Selection process: NA
	Time period	Study period : November 2003 - April 2008
Methods	Timing of assessment	Unclear
	Rating scale and clinical cut point for detecting depression	Geriatric Depression Scale (score \geq 21)

	Assessment methods	Face to face interviews (standardized data collection methods)
Results	Total number admissible	212
	Total number enrolled	199
	Number assessed/ response	199
	N(%) females of total sample	151(76%)
	Mean age (SD)	42.5±14.59
	Proportion of participants scoring above the cut point measure of depression	Information not available
Dennis et al., 1998 ¹⁶⁵		
Participant identification and recruitment	Country & Study design	UK, cross sectional study.
	Source of participants	Carers of stroke patients recruited over a two year period to a trial of a stroke family care worker. Exclusion criteria for stroke patients: 1) significant comorbidity 2) living > 25 miles away and 3) high risk of mortality within first few days.
	Assembly of cohort of carers or sample for cross sectional study	Sampling design: convenience sample. Definition of the informal care exposure: Not stated Criteria for determining informal carer exposure status: Not stated Eligibility criteria: Unclear Selection process: stroke survivors identified the main carer
	Time period	Unclear
Methods	Timing of assessment	6 months after initial assessment (within 30 days of stroke onset)
	Rating scale and clinical cut point for detecting	HADS (score ≥ 8)

	depression	
	Assessment methods	Self-completion questionnaire to be returned at later date
Results	Total number admissible	246
	Total number enrolled	Not applicable
	Number assessed/ response	222 (90.2%)
	N(%) females of total sample	148 (66%)
	Mean age (SD)	mean 60 (range 27 to 88 years)
	Proportion of participants scoring above the cut point measure of depression	42/185
Fatoye et al., 2006¹⁶⁶		
Participant identification and recruitment	Country & Study design	Nigeria, cross sectional study
	Source of participants	Consecutive sample of carers involved in caring for a stroke survivor for at least 3 months and were observed to be the main carer based on observations made in the hospital. Recruited between May 2004 and August 2005.
	Assembly of cohort of carers or sample for cross sectional study	Sampling design: consecutive sample. Definition of the informal care exposure: Unclear Criteria for determining informal carer exposure status: Unclear Eligibility criteria: Unclear Selection process: Unclear
	Time period	Recruited between May 2004 and August 2005
Methods	Timing of assessment	Duration of care giving \geq 3 months
	Rating scale and clinical cut point for detecting	HADs (score \geq 8)

	depression	
	Assessment methods	Unclear
Results	Total number admissible	103
	Total number enrolled	103
	Number assessed/ response	103
	N(%) females of total sample	68 (66%)
	Mean age (SD)	mean 41.2 (SD 3.9: range 20 to 65 years)
	Proportion of participants scoring above the cut point measure of depression	25/103
Grant et al., 2009¹⁶⁷		
Participant identification and recruitment	Country & Study design	USA, cohort study.
	Source of participants	Unclear
	Assembly of cohort of carers or sample for cross sectional study	Sampling design: Convenience sample of family members who were primarily responsible for assisting stroke patients with basic and instrumental activities of daily living. Definition of the informal care exposure: Not stated. Criteria for determining informal carer exposure status: unclear Eligibility criteria: Not stated Selection process: Unclear
	Time period	Unclear
Methods	Timing of assessment	1-2 days before discharge of the stroke survivor and 5, 9 and 13 weeks
	Rating scale and clinical cut point for detecting	CES-D 20 (score ≥ 20)

	depression	
	Assessment methods	Interview, measures administered in random order.
Results	Total number admissible	60
	Total number enrolled	52
	Number assessed/ response	48
	N(%) females of total sample	46 (88.5%)
	Mean age (SD)	56 (range 25-74 years)
	Proportion of participants scoring above the cut point measure of depression	1-2 days 19/52 (36.5%) 5 weeks 19/48 (39.5%)* 9 weeks 9/43 (20.3%) 13 weeks 14/41 (34%)
Greenwood et al., 2008¹⁶⁸		
Participant identification and recruitment	Country & Study design	UK, cohort study.
	Source of participants	Carers of stroke survivors recruited from one of two acute stroke units in South West London.
	Assembly of cohort of carers or sample for cross sectional study	Sampling design: Carers of consecutively admitted stroke patients. Definition of the informal care exposure: Not stated. Criteria for determining informal carer exposure status: Not stated. Eligibility criteria: carers had to be looking after stroke survivors either in the stroke survivor's home or the carers home. Selection process: Carers were identified by stroke survivors, staff or carers themselves.
	Time period	Two separate six month periods
Methods	Timing of assessment	Between discharge and 1 month (T1) Three months post discharge (T3)
	Rating scale and clinical cut point	HADs (score \geq 8)

	for detecting depression	
	Assessment methods	Interview
Results	Total number admissible	50
	Total number enrolled	47
	Number assessed/ response	45
	N(%) females of total sample	62.2%
	Mean age (SD)	Mean age unclear, approximately 50% aged less than 60 years.
	Proportion of participants scoring above the cut point measure of depression	T1 14/45 (31%) T2 13/45 (28.9%)*
Haley et al., 2009 ¹⁶⁹		
Participant identification and recruitment	Country & Study design	USA, cross sectional study
	Source of participants	<p>Potential recruits to the CARES are individuals previously enrolled in the REasons for Geographic and Racial Differences in Stroke (REGARDS) study. REGARDS is a national, population-based, longitudinal study of 30,000 African-American and white adults aged > or =45 years, recruited between January 2003 and October 2007. Participants are randomly sampled with recruitment by mail then telephone.</p> <p>CARES study enrolled stroke survivors and their family carers over a period of 36 months from August of 2005 to July of 2008.</p>
	Assembly of cohort of carers or sample for cross	<p>Sampling design: All carers of stroke survivors recruited to the REGARDS study.</p> <p>Definition of the informal care exposure: unclear</p> <p>Criteria for determining informal carer exposure</p>

	sectional study	status: unclear Eligibility criteria: (1) ≤ 21 years of age; or (2) able to comprehend or respond to study questions. Selection process: NA
	Time period	August of 2005 to July of 2008
Methods	Timing of assessment	8 to 12 months after stroke onset
	Rating scale and clinical cut point for detecting depression	CES-D-20 (score ≥ 16)
	Assessment methods	Telephone interviewing conducted by trained interviewers
Results	Total number admissible	230
	Total number enrolled	Not applicable
	Number assessed/ response	75 (32.6%)
	N(%) females of total sample	59 Female (79%)
	Mean age (SD)	63.69 (13.62)
	Proportion of participants scoring above the cut point measure of depression	10/75
King et al., 2001 ¹⁷⁰		
Participant identification and recruitment	Country & Study design	USA, cohort study
	Source of participants	Carers of stroke survivors were recruited from consecutive patient admissions over a period of 32 months to six hospitals.
	Assembly of cohort of carers or sample for	Sampling design: Consecutive sample of carers of first ever stroke patients consecutively admitted over a 32 month period. Definition of the informal care exposure: Not

	cross sectional study	stated Criteria for determining informal carer exposure status: unclear Eligibility criteria: Not stated Selection process: unclear
	Time period	Unclear
Methods	Timing of assessment	Prior to discharge (T1) and 6-10 weeks (T2) post discharge from hospital
	Rating scale and clinical cut point for detecting depression	CES-D 20 (score ≥ 16)
	Assessment methods	Interview
Results	Total number admissible	365
	Total number enrolled	174(48%)
	Number assessed/ response	T1 = 174 T2 = 136*
	N(%) females of total sample	66%
	Mean age (SD)	Data not available
	Proportion of participants scoring above the cut point measure of depression	(T1) 32/136 (24%) (T2) 28/136 (20%)*
Molloy et al., 2005⁶²		
Participant identification and recruitment	Country & Study design	UK, cohort study
	Source of participants	All stroke patients, discharged from hospital in Dundee, Scotland and their carers.
	Assembly of cohort of carers or sample for cross	Sampling design: All patients discharged from hospital and their carers. Definition of the informal care exposure: Not stated Criteria for determining informal carer exposure

	sectional study	status: the individual most involved in care of the stroke survivor at home. Eligibility criteria: Not stated Selection process: While stroke patients were in hospital and when their condition was assessed to be stable, patients were asked by a researcher to identify the person who was most involved in their care at home. Carers were identified at this point, contact details were sought and then carers were formally invited to participate.
	Time period	February 1998 and May 2000
Methods	Timing of assessment	2 weeks and 8 weeks post discharge from hospital
	Rating scale and clinical cut point for detecting depression	HADS (score ≥ 8)
	Assessment methods	In home face to face interviews
Results	Total number admissible	138
	Total number enrolled	Data available for 172 carers of stroke survivors. Data report. For 138 carer/ patient dyads for whom all data were available
	Number assessed/ response	2 weeks = 138 8 weeks =138*
	N(%) females of total sample	105/138(76%)
	Mean age (SD)	Mean 61.3 (SD 14; range 21 to 88)
	Proportion of participants scoring above the cut point measure of depression	Time 1(2 weeks after hospital discharge) 32/138(32%) Time 2(8 weeks after hospital discharge) 30/138*(30%)
Nir et al., 2009¹⁷¹		
Participant identification and recruitment	Country & Study design	Israel, cohort study
	Source of	Convenience sample of carers of stroke survivors

	participants	recruited to a trial of a structured nursing intervention
	Assembly of cohort of carers or sample for cross sectional study	Sampling design: convenience sample Definition of the informal care exposure: Not stated Criteria for determining informal carer exposure status: Not stated Selection process: Not stated
	Time period	Two year period
Methods	Timing of assessment	2 weeks post stroke, 3 and 6 months after stroke onset.
	Rating scale and clinical cut point for detecting depression	Short Geriatric Depression Scale (score ≥ 6)
	Assessment methods	Not clear
Results	Total number admissible	155
	Total number enrolled	140
	Number assessed/ response	137
	N(%) females of total sample	101 (72%)
	Mean age (SD)	Mean 55
	Proportion of participants scoring above the cut point measure of depression	53/140 at 2 weeks 42/137 at 3 months* 42/ 132 at 6 months
Rittman et al., 2006¹⁷²		
Participant identification and recruitment	Country & Study design	USA, cohort study
	Source of participants	Carers and stroke survivors were selected from geographically and ethnically diverse Veteran's Medical Affairs Centres in Florida, USA an Puerto

		Rico, South America
	Assembly of cohort of carers or sample for cross sectional study	Sampling design: All veteran stroke survivors discharged home following hospital care for stroke and their carers. Definition of the informal care exposure: Not stated Criteria for determining informal carer exposure status: Not stated Eligibility criteria: Not stated Selection process: Carers of stroke survivors either identified themselves or were identified by the stroke survivor
	Time period	2003 to 2006
Methods	Timing of assessment	1 month, 6 months, 12 months, 18 months, 24 months
	Rating scale and clinical cut point for detecting depression	GDS-30 \geq 11
	Assessment methods	Interview
Results	Total number admissible	Unclear
	Total number enrolled	135
	Number assessed/ response	1 month:119 6months:105
	N(%) females of total sample	Not available
	Mean age (SD)	Not available
	Proportion of participants scoring above the cut point measure of depression	1 month 24/119 (20.2%)* 6 months 17/105 (16.2%)
Schulz et al., 1988¹⁷³		
Participant identification and recruitment	Country & Study design	USA, cohort study

	Source of participants	Carers and stroke survivors identified from list of admissions to hospital or referral from rehabilitation specialists working in the hospitals
	Assembly of cohort of carers or sample for cross sectional study	Sampling design: All carers and stroke survivors identified from list of admissions to hospital or referral from rehabilitation specialists working in the hospitals Definition of the informal care exposure: not stated Criteria for determining informal carer exposure status: Not stated Eligibility criteria: Not stated. Selection process: unclear
	Time period	Unclear
Methods	Timing of assessment	7 weeks after stroke onset and 6 months later
	Rating scale and clinical cut point for detecting depression	CES-D-28 item (score ≥ 23)
	Assessment methods	Structured interview
Results	Total number admissible	186
	Total number enrolled	162 (85%)
	Number assessed/ response	140
	N(%) females of total sample	126 (78%)
	Mean age (SD)	56 (range 16 to 89 years)
	Proportion of participants scoring above the cut point measure of depression	7 weeks 55/162 (34%) 6 months 48/140 (34%)*
Shanmugham et al., 2009¹⁷⁴		
Participant identification	Country & Study	USA, cohort study

and recruitment	design	
	Source of participants	Carers of stroke patients discharged from a rehabilitation hospital in Philadelphia
	Assembly of cohort of carers or sample for cross sectional study	<p>Sampling design: Convenience sample of carers of stroke survivors about to be discharged from an inpatient rehabilitation hospital in Philadelphia and recruited to attend an education and training program on role as carer.</p> <p>Definition of the informal care exposure: Unclear</p> <p>Criteria for determining informal carer exposure status: Unclear</p> <p>Eligibility criteria: New to the care-giving role; provide services for the care recipient in their home.</p> <p>Selection Process: recruited from an education and training program on role as carer.</p>
	Time period	Unclear
Methods	Timing of assessment	Discharge and 1 month later
	Rating scale and clinical cut point for detecting depression	BDI-21(score ≥ 10)
	Assessment methods	Self-completion or completion by research assistant over telephone
Results	Total number admissible	Unclear
	Total number enrolled	43
	Number assessed/ response	43
	N(%) females of total sample	39(91%)
	Mean age (SD)	Unclear
	Proportion of participants scoring above the	<p>Discharge: 19/43 (44%)</p> <p>1 month after discharge: 19/43 (44%)*</p>

	cut point measure of depression	
Smith et al., 2004 ¹⁷⁵		
Participant identification and recruitment	Country & Study design	UK, cross sectional study
	Source of participants	Unpaid carers of stroke patients identified from stroke registers in two hospitals.
	Assembly of cohort of carers or sample for cross sectional study	Sampling design: convenience sample Definition of the informal care exposure: unclear Criteria for determining informal carer exposure status: Not stated. Eligibility criteria: Unclear Selection process: an identifiable carer providing physical, social and/ or emotional support. Carer identified by stroke patient.
	Time period	Unclear
Methods	Timing of assessment	One year after stroke onset
	Rating scale and clinical cut point for detecting depression	HADS (score ≥ 8)
	Assessment methods	Semi-structured taped interview
Results	Total number admissible	90
	Total number enrolled	Not applicable
	Number assessed/ response	89(99%)
	N(%) females of total sample	65(75.2%)
	Mean age (SD)	57.8 (range 19-84 years)
	Proportion of participants scoring above the cut point	17/89

	measure of depression	
Teel et al., 2001 ¹⁷⁶		
Participant identification and recruitment	Country & Study design	USA, cohort study
	Source of participants	Carers of stroke patients in the Kansas City Stroke Study admitted to one of 12 participating city hospitals in the Kansas City area. The primary family carers for the first 302 stroke patients were invited to participate in the study.
	Assembly of cohort of carers or sample for cross sectional study	Sampling design: Convenience sample of carers of stroke patients admitted to one of 12 hospitals in Greater Kansas City area Definition of the informal care exposure: A family member or friend taking primary responsibility for managing the aftercare of the person with stroke. Criteria for determining informal carer exposure status: Eligibility criteria: Family member or friend taking primary responsibility for managing the aftercare of the stroke survivor; 18 years of age and above; and fluent in English. Selection process: At initial telephone contact, each potential participant was confirmed to be the primary care-giver.
	Time period	Unclear
Methods	Timing of assessment	1 month, 3 month and 6 months after stroke onset
	Rating scale and clinical cut point for detecting depression	CES-D. No information on clinical cut point available.
	Assessment methods	Mailed questionnaire
Results	Total number admissible	302
	Total number enrolled	Unclear
	Number assessed/ response	83
	N(%) females of	59 (71.1%)

	total sample	
	Mean age (SD)	Mean 57 (SD 14.2)
	Proportion of participants scoring above the cut point measure of depression	Not available

Table 4-3 Characteristics of excluded studies

Study	Reason for exclusion
Anderson 1995 ³⁵	Subgroup of stroke survivors (Oxford Handicap Scale 3, 4, 5).
Anderson 1997 ¹⁷⁹	Study examining the association between carers coping style and depression.
Blake 2003 ¹⁸⁰	47% all admissible participants included/ subgroup (spouses).
Blonder 2007 ¹⁸¹	Study examining the association between stroke survivors neurobehavioral characteristics and depression in carers.
Bluvol 2004 ¹⁸²	Not study of people providing care to stroke survivors.
Braithwaite 1993 ¹⁸³	Study examining the association between carers (of stroke survivors) emotional distress and ability to learn.
Brocklehurst 1981 ¹⁸⁴	Study does not use a standardised rating scale for depression.
Bruun Wyller 2003 ¹⁸⁵	Study of the effect on relatives of stroke survivors not carers of stroke survivors.
Cameron 2011 ¹⁸⁶	Prospective cohort study of stroke survivors, carer assessment at 18 and 24 months post stroke.
Carnwath 1987 ¹⁸⁷	Study of subgroup of carers (spouse).
Carod Artal 2009 ¹⁸⁸	Carers assessed at the time stroke patients admitted to a rehabilitation hospital i.e., not living in at a permanent address in the community.
Choi-Kwon 2005 ¹⁸⁹	Study of subgroup of stroke survivors (Live-in).
Chow 2006 ¹⁹⁰	Study uses a depression measure with no recognised clinical cut point for Chinese population
Christopher 1999 ¹⁹¹	Study does not use a standardised rating scale for depression.
Chumbler 2004 ¹⁹²	Link to Rittman 2006

Study	Reason for exclusion
Clark 2002 ¹⁹³	Study examining the association between carers (of stroke survivors) hardiness and depression.
Cuellar 2002 ¹⁹⁴	Study of subgroup of carers (females)
Davis 1997 ¹⁹⁵	Study examining the association between stroke survivor, carer characteristics and depression in wives of stroke survivors
Draper 1992 ¹⁹⁶	Study of subgroup of carers (live-in)
Draper 2005 ¹⁹⁷	Study of subgroup of carers (spouse)
Epstein-Lublow 2009 ¹⁹⁸	Data from a baseline assessment of an intervention study
Evans 1989 ¹⁹⁹	Not depression
Fitzgerald 1989 ²⁰⁰	Study of subgroup of carers (spouse)
Forsberg Wårleby 2001 ²⁰¹	Not depression
Forsberg Wårleby 2004 ²⁰²	Not depression
Franzén Dhalin 2007 ²⁰³	Study of subgroup of carers (spouse)
Fredman 1997 ²⁰⁴	Not stroke specific
Garcia 1999 ²⁰⁵	Not depression
Grabowska-Fudala 2007 ²⁰⁶	Analytic survey
Green 2007 ²⁰⁷	Study of subgroup of carers (spouse)
Greveson 1991 ²⁰⁸	Not depression
Gosman-Hedström 2008 ²⁰⁹	Study of subgroup of carers (spouse)
Hershkowitz 1990 ²¹¹	Study examined the relationship between psychosocial variables and psychological adaptation of stroke patients and their spouse/carers
Hochstenbach 2005 ²¹²	Study to quantify the agreement between carers and survivors on reported changes in physical, emotional, behavioural and cognitive changes.
Hodgson 1996 ²¹³	Not depression
Hop 2002 ²¹⁴	Study of stroke subgroup (subarachnoid haemorrhage)
Huang 2009 ²¹⁵	Study of relations between care-giving and a number of variables. Convenience sample.
Hung 2007 ²¹⁶	Study of the relation between care-giver pain and depression on stroke survivor
Ilse 2008 ²¹⁷	Not depression
Jeng-Ru 1998 ²¹⁸	Not depression
Jones 2000 ²¹⁹	Not depression
Jönsson 2005 ²²⁰	Not depression
Jorstad 2004 ²²¹	Study examined the relationship between life changes associated with providing care to a stroke survivor and depression in the carer.
Jungbauer 2003 ²²²	Study of subgroup of carers (spouse)
King 1995 ²²³	Study compares dyads of stroke survivor/ primary support persons on various characteristics.
Kinney 1995 ²²⁴	Study aims to identify stresses and satisfactions

Study	Reason for exclusion
	associated with providing care to a stroke survivor and to examine the relationship between stresses and satisfactions with three outcomes, one of which is depression.
Kitze 2002 ²²⁵	Study of subgroup of carers (spouse)
Ko 2007 ²²⁶	Secondary analysis of data from the Family Function, Stroke Recovery and Carer outcomes study.
Kotila 1998 ²²⁷	Multiple sub-groups of stroke survivors and carers (comparison of depression in carers in active districts versus non-active districts in Finland).
Larson 2005 ²²⁸	Not depression.
Li 2004 ²²⁹	Not depression.
Li 2005 ²³⁰	Exploratory study.
Liu 2002 ²³¹	Multiple sub-groups of stroke survivors and carers (comparison of depression in carers in active districts versus non-active districts in China).
Macnamara 1985 ²³²	Study of subgroup of carers (spouses).
Macnamara 1990 ²³³	No recognised cut point for depression.
Matson 1994 ²³⁴	Less than 80% carers of stroke survivors.
McLenahan 1998 ²³⁵	Survey.
McLean 1991 ²³⁶	Survey.
Morimoto 2003 ²³⁷	Study of sub group of carers (live-in)
Muraki 2008 ²³⁸	Not depression
Nakipoglu 2006 ²³⁹	Aim of study was to evaluate and compare the depressive mood findings in geriatric hemiplegic patients and geriatric carers of the patients.
Nelson 2008 ²⁴⁰	Not depression
Nieboer 1998 ²⁴¹	Study of subgroup of carers (spouse)
Ozge 2009 ²⁴²	Study of subgroup of carers (live-in)
Parag 2008 ²⁴³	Not depression
Park 2006 ²⁴⁴	Study explores factors related to well-being of family members
Perrin 2009 ²⁴⁵	Link to Rittman
Potter 2003 ²⁴⁶	Survey of 45 self-identified carers of traumatic brain injury and stroke survivors.
Pritchard 2001 ²⁴⁷	Study of stroke subgroup (aneurysmal subarachnoid haemorrhage)
Qiu 2008 ²⁴⁸	Study aim was to identify coping strategies of stroke survivors
Rau 1986 ²⁴⁹	Study of subgroup of carers (partners)
Reese 1994 ²⁵⁰	Study compares 25 carers of stroke survivors and 25 carers of people with Alzheimers disease with 25 non carers on psychologic and immunologic indices.
Rigby 2009 ²⁵¹	Not depression
Rittman 2009 ²⁵²	Study explores and describes sleep experience of informal carers of stroke survivors.
Rochette 2007 ²⁵³	Study of subgroup of carers (spouse)
Schlote 1998 ²⁵⁴	Not depression

Study	Reason for exclusion
Schlote 2006 ²⁵⁵	Not depression
Schriener 2006* ²⁵⁶	Other (link to Morimoto)
Silliman 1986 ²⁵⁷	Study of subgroup of carers (live-in)
Simon 2009 ²⁵⁸	Study of subgroup of carers (live-in)
Ski 2007 ²⁵⁹	Study of subgroup of carers (live-in)
Smith 2003 ²⁶⁰	Randomised controlled trial
Stein 1992 ²⁶¹	Study of subgroup of carers (spouse)
Steiner 2008 ²⁶²	Descriptive comparative study
Stevens 1996 ²⁶³	Descriptive comparative study
Stone 2004 ²⁶⁴	Study to examine carers assessment of personality change in stroke patients.
Suh 2004 ²⁶⁵	Descriptive comparative study
Thommesen 2002 ²⁶⁵	Study of subgroup of carers (spouse)
Thompson 1990 ²⁶⁶	Study investigates factors associated with depression in carers of stroke survivors, participants selected on the basis of exposure.
Tooth 2005 ²⁶⁷	Not depression
Visser Meily 2005 ²⁶⁸	Study of subgroup of carers (spouse)
Visser Meily 2008 ²⁶⁹	Study of subgroup of carers (spouse)
Wade 1986 ²⁷⁰	Study of subgroup of carers (live-in)
Watanabe 2003 ²⁷¹	Study carried out while stroke patients still in hospital
White 2003 ²⁷²	Not depression
White 2006 ²⁷³	Not depression
Williams 1993 ²⁷⁴	Descriptive study
Wilz 2008 ²⁷⁵	Not depression
Wright 1999 ²⁷⁶	Study of subgroup of carers (spouse)
Yeung 2007 ²⁷⁷	Descriptive study
Zak 1999 ²⁷⁸	Study of subgroup of carers(spouse)

Table 4-4: Critical appraisal of studies included in this review

Filled squares represent features present; clear squares represent features not present; ? represents unknown data; NA represents data not available; NR represents not relevant for the particular study design.

Study	Definition of informal care Exposure?	Participants defined?	% of admissible participants recruited	Participants generalizable?	Adequacy of ascertainment of the informal care exposure	Evidence Participants recruited early in exposure	Evidence Outcome not present at start of study	Outcome				Socio-demographic risk factors/ correlates assessed			
								Blinded assessment of outcome	Follow-up at least 3 months? (cohort studies)	Adequate follow-up? (Cohort studies ≥ 80%)	Standardised data collection methods	Age	Gender	Ethnic group	Socioeconomic status
Bakas 2006 ¹⁶⁰	<input type="checkbox"/>	<input type="checkbox"/>	?	<input type="checkbox"/>	■	<input type="checkbox"/>	<input type="checkbox"/>	?	■	■	?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Berg 2006 ¹⁶¹	<input type="checkbox"/>	<input type="checkbox"/>	100%	■	?	<input type="checkbox"/>	<input type="checkbox"/>	?	■	■	■	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Cameron 2006 ¹⁶²	<input type="checkbox"/>	■	66%	<input type="checkbox"/>	■	NR	NR	NR	NR	NR	<input type="checkbox"/>	NR	NR	NR	<input type="checkbox"/>
Cumming 2004 ¹⁶³	<input type="checkbox"/>	■	89%	<input type="checkbox"/>	?	<input type="checkbox"/>	<input type="checkbox"/>	?	■	<input type="checkbox"/>	<input type="checkbox"/>	■	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Das 2010 ¹⁶⁴	■	■	94%	■	?	NR	NR	NR	NR	NR	■	NR	NR	NR	<input type="checkbox"/>
Dennis 2007 ¹⁶⁵	<input type="checkbox"/>	■	90%	<input type="checkbox"/>	?	NR	NR	NR	NR	NR	■	NR	NR	NR	<input type="checkbox"/>
Fatoye 2006 ¹⁶⁶	<input type="checkbox"/>	■	100%	■	?	NR	NR	NR	NR	NR	■	NR	NR	NR	<input type="checkbox"/>
Grant 2004 ¹⁶⁷	<input type="checkbox"/>	<input type="checkbox"/>	85%	<input type="checkbox"/>	?	<input type="checkbox"/>	<input type="checkbox"/>	?	■	■	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	■	<input type="checkbox"/>
Greenwood 2008 ¹⁶⁸	<input type="checkbox"/>	<input type="checkbox"/>	94%	■	?	?	<input type="checkbox"/>	?	■	■	■	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Haley 200 ¹⁶⁹	<input type="checkbox"/>	■	33%	<input type="checkbox"/>	?	NR	NR	NR	NR	NR	■	NR	NR	NR	<input type="checkbox"/>
King 2001 ¹⁷⁰	<input type="checkbox"/>	<input type="checkbox"/>	48%	<input type="checkbox"/>	?	<input type="checkbox"/>	<input type="checkbox"/>	?	<input type="checkbox"/>	<input type="checkbox"/>	■	■	■	<input type="checkbox"/>	<input type="checkbox"/>
Molloy 2003 ⁶²	<input type="checkbox"/>	■	?	<input type="checkbox"/>	?	<input type="checkbox"/>	<input type="checkbox"/>	?	<input type="checkbox"/>	■	?	■	■	<input type="checkbox"/>	<input type="checkbox"/>
Nir 2009 ¹⁷¹	<input type="checkbox"/>	■	?	<input type="checkbox"/>	?	<input type="checkbox"/>	<input type="checkbox"/>	?	■	?	?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Rittman 2006 ¹⁷²	<input type="checkbox"/>	?	?	<input type="checkbox"/>	?	<input type="checkbox"/>	<input type="checkbox"/>	?	■	?	■	NA	NA	NA	NA
Schulz 1988 ¹⁷³	<input type="checkbox"/>	■	85%	■	?	<input type="checkbox"/>	<input type="checkbox"/>	?	■	■	■	■	<input type="checkbox"/>	<input type="checkbox"/>	■
Shanmugham 2009 ¹⁷⁴	<input type="checkbox"/>	<input type="checkbox"/>	?	<input type="checkbox"/>	?	■	<input type="checkbox"/>	■	<input type="checkbox"/>	■	<input type="checkbox"/>	■	■	<input type="checkbox"/>	<input type="checkbox"/>
Smith 2004 ¹⁷⁵	<input type="checkbox"/>	<input type="checkbox"/>	99%	<input type="checkbox"/>	?	NR	NR	NR	NR	NR	■	NR	NR	NR	<input type="checkbox"/>
Teel 2001 ¹⁷⁶	<input type="checkbox"/>	<input type="checkbox"/>	49%	<input type="checkbox"/>	?	<input type="checkbox"/>	<input type="checkbox"/>	■	■	■	■	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Table 4-5: Influence of demographic, care-giver, care-giving and stroke survivor factors on prevalence on depression in people who provide care to stroke survivors

r represents the correlation coefficient; β represents the β regression co-efficient; SE represents standard error; OR represents odds ratio; NS represents non-significant; 95% CI represents 95% confidence interval.

Correlation coefficients (*r*) presented represent the association of the two variables measured and assessed at follow-up time only.

Study	Berg 2005 ¹⁶¹	Cumming 2004 ¹⁶³	Grant 2004 ¹⁶⁷	King 2001 ¹⁷⁰	Molloy 2005 ⁶²	Schulz 1988 ¹⁷³	Shanmugham 2009 ¹⁷⁴
Follow-up period	6 months after acute stroke	3 years post stroke onset	1-2 days prior to discharge	6 - 10 weeks post-discharge	8 weeks post-discharge	8 months after stroke onset	1 month after discharge
Carer demographic factors							
<i>Age</i>	-	NS	-	$r = -.13$ (NS)	Time 1 $\beta =$ NS Time 2 $\beta =$ NS	$r = -.3$ (NS)	NS
<i>Gender</i>	-			Female sex $r = -.23$ ($p < 0.01$)	Time 1 $\beta =$ NS Time 2 $\beta =$ NS	-	NS
<i>Ethnic group</i>	-	-	- White OR 3.7 ($p =$ 0.04)	-	-	-	-
<i>Marital status</i>	-	-	-	-	-	-	-
<i>Education</i>	-	-	-	-	-	-	NS

Study	Berg 2005 ¹⁶¹	Cumming 2004 ¹⁶³	Grant 2004 ¹⁶⁷	King 2001 ¹⁷⁰	Molloy 2005 ⁶²	Schulz 1988 ¹⁷³	Shanmugham 2009 ¹⁷⁴
Follow-up period	6 months after acute stroke	3 years post stroke onset	1-2 days prior to discharge	6 - 10 weeks post-discharge	8 weeks post-discharge	8 months after stroke onset	1 month after discharge
Employment	-	Not presented	-	$r = -.06(NS)$	-	-	-
Income	-	-	-	-	-	$r = -.34(NS)$	-
Carer health							
General Health	-	-	NS	$r = .25$ ($p < 0.01$)	-	-	-
Positive well-being at follow-up	-	-	-	-	-	$r = -.39(NS)$	-
Negative well-being at follow-up	-	-	-	-	-	$r = .55(NS)$	-
Objective health problems at follow-up	-	-	-	-	-	$r = .26(NS)$	-
Subjective health problems at follow-up	-	-	-	-	-	$r = .35(NS)$	-
Carer attributes or skills							
Cognitive appraisal impact	-	-	-	$r = .47$ ($p < 0.01$)	-	-	-
Comprimising coping	-	-	-	$r = .24$ ($p < 0.01$)	-	-	-
Avoidant coping	-	-	-	$r = .17(NS)$	-	-	-
Cautious coping	-	-	-	$r = .15(NS)$	-	-	-
Social support coping	-	-	-	$r = .15(NS)$	-	-	-
Care-giving factors							
Relationship to survivor	-	NS	-	-.14 (NS)	Spouses vs other Time 1 B =	-	NS

Study	Berg 2005 ¹⁶¹	Cumming 2004 ¹⁶³	Grant 2004 ¹⁶⁷	King 2001 ¹⁷⁰	Molloy 2005 ⁶²	Schulz 1988 ¹⁷³	Shanmugham 2009 ¹⁷⁴
Follow-up period	6 months after acute stroke	3 years post stroke onset	1-2 days prior to discharge	6 - 10 weeks post-discharge	8 weeks post-discharge	8 months after stroke onset	1 month after discharge
					.19 (NS) Time 2 β = .21 (NS)($p < .05$)		
Demand	-	-	-	-	T1 Higher demand β = .20($p < .01$) lower control β = -.27($p < .01$) Time 2 lower control β = -.33 ($p < .01$)	-	-
Carer burden	-	-	OR = 1.05 (p = 0.01)	-	-	r = .56(NS)	-
Family functioning	-	-	-	r = .16(NS)	-	-	-
Tangible support	-	-	-	r = -.16(NS)	-	-	-
Social support	-	β = -.674 (SE .237; $p < 0.004$) OR = 0.51(95% CI 0.32, 0.81)	-	-	-	-	-
Social support - belonging	-	-	OR = 0.70 (< 0.01)	-	-	-	-

Study	Berg 2005 ¹⁶¹	Cumming 2004 ¹⁶³	Grant 2004 ¹⁶⁷	King 2001 ¹⁷⁰	Molloy 2005 ⁶²	Schulz 1988 ¹⁷³	Shanmugham 2009 ¹⁷⁴
Follow-up period	6 months after acute stroke	3 years post stroke onset	1-2 days prior to discharge	6 - 10 weeks post-discharge	8 weeks post-discharge	8 months after stroke onset	1 month after discharge
Perceived severity of stroke	-	-	-	-	-	$r = .23(p>0.01)$	-
Concern about another stroke	-	-	-	-	-	$r = .04(p>0.01)$	-
Carer personal life							
Good marital relationship at follow-up	-	-	-	-	-	$r = -.04(p<0.01)$	-
Poor marital relationship at follow-up	-	-	-	-	-	$r = .27(p<0.01)$	-
Satisfaction with amount of social contact at follow-up	-	-	-	-	-	$r = -.10(p<0.05)$	-
Satisfaction with quality of social contact at follow-up	-	-	-	-	-	$r = -.09(p<0.05)$	-
Stroke survivor factors							
Age	NS	-	-	-	-	-	-
Gender	Male sex ($p < 0.05$)	-	-	-	-	-	-
Stroke severity	NS	-	-	-	-	-	-
6 month Barthel Index	NS	-	-	-	-	-	-
8 month Barthel Index	-	-	-	-	-	$r = -.02(p<0.01)$	-

Study	Berg 2005 ¹⁶¹	Cumming 2004 ¹⁶³	Grant 2004 ¹⁶⁷	King 2001 ¹⁷⁰	Molloy 2005 ⁶²	Schulz 1988 ¹⁷³	Shanmugham 2009 ¹⁷⁴
Follow-up period	6 months after acute stroke	3 years post stroke onset	1-2 days prior to discharge	6 - 10 weeks post-discharge	8 weeks post-discharge	8 months after stroke onset	1 month after discharge
18 month Barthel Index	NS	-	-	-	-	-	-
3 year Barthel Index	-	Not presented	-	-	-	-	-
Irritability, depression & anxiety	-	$\beta = .085$ (SE .031; $p = .007$) OR = 1.09 (95% CI 1.02, 1.16)	-	-	-	-	-
London Handicap Scale	-	Not presented	-	-	-	-	-
Survivor co-morbidity	-	-	-	0.12(NS)	-	-	-
Stroke survivor communication	-	-	-	-	-	-	-

Chapter 5 Non pharmacological interventions for informal carers of stroke survivors

5.1 Introduction

Prevailing wisdom is that providing informal care to a stroke survivor is burdensome, depressing and provokes anxiety. Further evidence (chapter 3) suggests that being exposed to providing informal care and may be associated with increased perceived stress and a reduction in psychological well-being.

The question is can anything be done to promote a persons ability to cope in the face of having to provide what is necessary for the health, well-being, maintenance or safety of a stroke survivor?

5.2 Background (A)

An informal carer (or unpaid carer) has been defined as 'a person of any age who provides unpaid help and support to a relative, friend or neighbour who cannot manage to live independently without the carers help due to frailty, illness, disability or addiction'²⁸⁹.

Informal carers play an important and sizeable part in the total care provided to stroke survivors. Informal carers often provide significant amounts of assistance with personal and instrumental activities of daily living: they monitor signs and symptoms and general health; store, control and appropriately administer medications; organise and co-ordinate care among health and social care providers; act as an advocate for the care recipient; and provide emotional and psychosocial support. Therefore, the care giving scenario can be complex, demanding and challenging.

Providing informal unpaid care, help, or support to stroke survivors who live in the community can be burdensome²⁹⁰ and stressful¹⁷⁵, and can have an adverse effect on the carer's psychological well being^{161;227} and physical health¹⁸⁷.

A range of healthcare interventions targeted towards stroke survivors and their family or other informal carers has been tested in randomised controlled trials (RCTs).

The aim of this systematic review and meta-analysis was to determine more clearly the effects of interventions directed towards the informal carer, the care giving working conditions (e.g. typical hours of care provided, flexibility, the nature of care giving tasks performed, the physical environment, the physical, emotional and mental demands, autonomy in decision making, training opportunities, availability of professional support etc) or interventions that target both carer and care giving working conditions on a range of outcomes.

5.2.1 Description of the condition

An increasing number of studies have found an association between stress in informal carers and immune dysregulation⁶⁴, an increased risk of mortality²⁹, elevated blood pressure³⁹, impaired wound healing³⁶, increased risk of coronary heart disease³⁰, and poorer cognitive function⁴² among women who provide care to their disabled or ill spouses.

The hypothesis is that when the demands placed on the informal carer are at variance with the needs, expectations and capacity of the carer, this stress can predispose the carer to ill health.

5.2.2 Description of the intervention

This review focused on any intervention targeted towards the carer or the care giving working conditions, or interventions that target the combination of carer and care giving working conditions.

5.2.3 How the intervention might work

These interventions might work to reduce the care giving demands through:

- changing the knowledge, beliefs, attitudes or behaviours of the carer; or

- temporarily reducing or removing the carer's responsibility for the stroke survivor; or
- addressing ongoing psychological and social problems.

5.2.4 Why it is important to do this review

Given that carers provide a substantial amount of the overall care delivered to stroke survivors and are likely to be at risk of adverse health outcomes, it would be useful for healthcare professionals, informal carers as well as those responsible for the disbursement of health and social care resources to have easy access to this information, to prevent further associated morbidity. Furthermore, aspects of the health of carers are addressed in several Cochrane Reviews; however, the carers are not the primary focus of any review.

Objectives

The objective of this review was to provide the most reliable summary of the effect of interventions targeted towards informal carers of stroke survivors or targeted towards informal carers and the care recipient (the stroke survivor). The specific questions were as follows:

- What are the effects of interventions targeted towards informal carers of stroke survivors?
- Is the evidence of benefit greater in any pre-defined subgroup?

5.3 Methods (B)

5.3.1 Criteria for considering studies for this review

5.3.1.1 Types of studies

All truly randomised controlled trials (RCT) of non-pharmacological interventions targeted towards informal carers of stroke survivors with the aim of either: changing knowledge, beliefs, attitude or behaviours of the informal carer, or temporarily reducing/removing the carer's responsibility for the stroke survivor were sought. Studies which include stroke survivors and carers were excluded if the stroke survivors were the primary target of the intervention.

5.3.1.2 **Types of participants**

Trials that recruit informal carers of stroke patients were included. A definition of an informal carer is 'a person of any age who provides one or more hours of unpaid help and support per week to a stroke survivor'. However, for the purpose of this review, the investigators' definition was accepted. Trials of mixed aetiology if the percentage of stroke patients was less than 80% were excluded.

5.3.1.3 **Types of interventions**

The review focused on trials of non-pharmacological interventions, compared with no care or routine care that has the following features:

- delivered to an informal carer of a stroke survivor;
- delivered to an informal carer and a stroke survivor as a dyad, that is, both informal carer and stroke survivor are randomised;
- where there is an intention to have an impact on carers' knowledge, beliefs, attitude or behaviour

Trials of non-pharmacological interventions where there is an intention to reduce or remove the responsibility for care giving, for example, through the provision of external support services (such as home help, day care, respite care, support groups, etc), or the means by which to employ external support were eligible for inclusion.

Trials of any non-pharmacological intervention were sought regardless of who provided the intervention (e.g. OT, PT, nurse, etc) or the type of intervention (e.g. educational, counselling, etc) or amount of intervention delivered.

5.3.1.4 **Types of outcome measures**

5.3.1.4.1 **Primary outcomes**

- Informal carer stress and strain (e.g. Carer Strain Index⁸⁹) at the end of scheduled follow up.
- Informal carer well being at the end of scheduled follow up (e.g. Carer Well-Being Scale)

5.3.1.4.2 **Secondary outcomes**

- Global measures of stress or distress. Lying above or below the median cut-off point²⁹¹ on global measures of stress or psychological distress (e.g. General Health Questionnaire (GHQ), Global measures of Perceived Stress Scale²⁹². If cut-off values are not available, then we will use the available mean scores and standard deviation.
- Measures of anxiety. Lying above or below the cut-off point (e.g. Hospital Anxiety and Depression Scale (HADS) cut-off point greater than 11 is a 'severely' disordered state of anxiety). If cut-off values were not available then available mean scores and standard deviations were used.
- Measures of depression (e.g. HADS cut-off point greater than 11 is a 'severely' disordered state of depression). If cut-off values were not available then available mean scores and standard deviations were used. Informal carer health-related quality of life at the end of scheduled follow up (e.g. Nottingham Health Profile (NHP)).
- Informal carer satisfaction.
- Informal carer mortality.

5.3.2 Search methods for identification of studies

See the 'Specialized register' section in the Cochrane Stroke Group module.

5.3.2.1 Electronic searches

The Cochrane Stroke Group Trials Register was last searched in March 2011. In addition the following electronic bibliographic databases were searched:

- The Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library, Issue 4 2010)
- MEDLINE (1948 to April 2011) (Appendix 15)
- EMBASE (1980 to April 2011) (Appendix 16)
- CINAHL (1982 to April 2011) (Appendix 17)
- AMED (Allied and Complementary Medicine) (1985 to August 2010)
- PsycINFO (1967 to April 2011)
- AARP (AgeLine) (1987 to December 2009)
- British Nursing Index and Archive (1985 to July 2010)
- Proquest Dissertations and Theses (1861 to August 2010)

- EMBASE Classic (1947 to 1973)
- HMIC Health Management and Information Consortium (1979 to March 2011)
- Social Work Abstracts (1968 to August 2010)
- Science Citation Index Expanded (SCI-Expanded)(ISI Web of Science 1990 to August 2010), Social Sciences Citation Index (SSCI)(ISI Web of Science 1956 to August 2010), Arts & Humanities Citation Index (A&HCI)(ISI Web of Science 1975 to August 2010), Conference Proceedings Citation Index - Science (CPCI-S)(ISI Web of Science 1990 to August 2010), Conference Proceedings Citation Index - Social Sciences & Humanities (CPCI-SSH)(ISI Web of Science 1990 to August 2010).

The search strategies were developed in conjunction with the Cochrane Stroke Group Trials Search Co-ordinator and adapted the MEDLINE strategy for the other databases.

5.3.2.2 Searching other resources

In an effort to identify further published, unpublished and ongoing trials:

(a) the following conference proceedings were searched:

European Stroke Conference (2006, 2007, 2008, 2009, 2010)

World Stroke Congress (2006, 2008, 2010)

UK Stroke Forum (2006, 2007, 2008, 2009, 2010)

(b) the following ongoing trials registers were searched

- Stroke Trials Registry (<http://www.strokecenter.org/trials/>) (18th March 2010)
- Clinical trials.gov (<http://clinicaltrials.gov/>) (16th March 2010)
- Australia New Zealand Clinical Trials Registry (<http://anzctr.org.au/trial>) (5th April 2010)

(c) the following archived research

- registers were searched
- National Research Register (<http://portal.nihr.ac.uk/>) (13th March 2008)

(d) the reference lists of relevant articles were searched

(e) authors and researchers in the field were contacted.

Trials in all languages were searched for. Translation was arranged for relevant studies published in languages other than English.

5.3.3 Data collection and analysis

5.3.3.1 Selection of studies

One review author (LL) screened all the titles, abstracts and keywords of publications identified by the searches to assess their eligibility. At this stage, studies that clearly did not meet the inclusion criteria were excluded. A paper copy of the full publication for every study that was potentially relevant was obtained. LL and one other review author (PL, TQ or FM) applied the selection criteria to each study identified by the search strategy. Disagreements were resolved by consensus.

5.3.4 Data extraction and management

Published and unpublished data were sought for this review. Two review authors independently extracted the data using a standard data recording form (LL, TQ and FM). The features of interest in parallel trials were sequence generation, allocation sequence concealment, blinding, incomplete outcome data, and selective outcome reporting and other potential sources of bias. All review authors (TQ, PL, LN, DS, FM and JT) participated in a blinded assessment of trial methods using the Cochrane Collaborations tool for assessing risk of bias. Each trial was determined to be at high or low risk of bias according to guidance suggested by the Cochrane Collaboration. Disagreements were resolved by discussion.

5.3.5 Assessment of risk of bias in included studies

For each included trial we extracted information about the method of randomisation and allocation concealment, blinding of outcome assessment, whether all the randomised patients were accounted for in the analysis and presence of selective outcome reporting.

5.3.6 Measures of treatment effect

5.3.6.1 Continuous outcomes

All outcomes within this review, with the exception of mortality, are continuous outcomes. However, for the purposes of the review, only informal carer stress and strain, informal carer well-being (the primary outcomes), depression, health related quality of life and satisfaction (secondary outcomes) were analysed as continuous variables, using means and standard deviations, under the assumption that the data have a Normal distribution.

5.3.6.2 Dichotomous outcomes

This review also includes dichotomous data, that is data from outcomes that can be split into two discrete categories, each trial participant must be in one state or the other, and cannot be in both categories. There are two types of dichotomous outcomes in this review: dichotomous data (alive or dead) and data that have been dichotomised from outcomes that are not truly dichotomous. For the purposes of this review the psychometric measures of stress or distress, depression and measures of anxiety have been converted to dichotomous data using published optimal clinical cut points. The optimal cut-point is a value in an ordered sequence of values that is used to separate those individuals who are in one state versus another state. For example, those participants who lie above the clinical cut point on a depression scale are likely to meet mood disorder diagnostic criteria for depression and those who lie below the cut point are unlikely to be distressed. The effect measure of choice for dichotomous outcomes was the risk ratio (RR).

5.3.7 Unit of analysis issues

The focus of this review was on trials that randomised individual carers or carer and stroke survivor dyads. In the event we had included a trial using a cluster design (in which participants were randomised at group level) we would have used the intra-cluster correlation coefficient (ICC) to estimate the effective sample size.

5.3.8 Dealing with missing data

This review focused on trials that have randomised individual carers or carer and stroke survivor dyads.

The primary aim of this review was to obtain standardised data through collaboration with the original trialists. Where data were missing from a published report the primary investigators were contacted in an attempt to get this information. Incomplete data are relatively common in trials of rehabilitation. It is difficult to impute missing values for continuous outcomes.

5.3.9 Assessment of heterogeneity

Heterogeneity was assessed by visually examining forest plots, by performing the ("chi-squared") test using a p-value of less than 0.1 to indicate heterogeneity. P-value of less than 0.1 was used rather than the conventional cut point of 0.05 because of the low power of this test. The effect of heterogeneity was quantified using the I^2 statistic including its 95% CI. The I^2 statistic is a measure of the degree of inconsistency in the studies' results. The value of the I^2 statistic ranges from 0% to 100% with 0% representing no observed heterogeneity to larger number representing increasing heterogeneity²⁹³. An I^2 value greater than 50% was considered substantial inconsistency¹²⁷.

5.3.10 Assessment of reporting biases

Funnel plot asymmetry was not tested for as there were fewer than 10 studies included in the meta-analysis²⁹³.

5.3.11 Data synthesis

A fixed effects model²⁹⁴ and random effects model²⁹⁵ were used to assess the sensitivity of results to choice of model.

5.3.12 Subgroup analysis and investigation of heterogeneity

The studies included in this review are clinically, methodologically and statistically heterogeneous therefore it was decided that it was not appropriate to perform subgroup analysis.

5.3.13 Sensitivity analysis

A sensitivity analyses was planned to explore the influence of study design factors including sequence generation, allocation sequence concealment, blinding of outcome assessor and presence of intention-to-treat analysis to determine how robust the analyses are. However, it was decided that the planned sensitivity analyses were not appropriate due to the diverse clinical and methodological nature of the studies.

5.4 Results (C)

5.4.1 Description of studies

5.4.1.1 Results of the search

The search strategy identified 22713 citations. Title and abstract screening identified 87 manuscripts and trial records as potentially eligible for this review. The full text screening excluded 65 manuscripts. See Figure 5-1.

Of the remaining 22 studies, the main contacts for two completed trials identified from clinical trial registers were contacted for further information without any success²⁹⁶⁻²⁹⁸ and one contact person for another completed trial could not be traced²⁹⁹⁻³⁰⁰ (see table 5-4 Characteristics of studies awaiting assessment); 11 studies are ongoing³⁰¹⁻³¹² (see table 5-3 Characteristics of ongoing studies) . Of the remaining eight studies^{63; 313-320} seven authors were

contacted for further details on study methods and outcome data^{63; 313-319}. Data from one study published in Korean³²⁰ was abstracted by a Korean speaking person. There were insufficient resources to get more information than was available from the published paper. Only one author failed to respond the request for further information³¹⁵.

5.4.1.1.1 *Included studies*

Eight studies^{63; 313-320} including a total of 1007 participants met the inclusion criteria. Detailed information about each is shown in the table 5-1

Characteristics of included studies. Seven studies^{63; 313-319} were published in English. One study was published in Korean³²⁰.

5.4.1.1.2 *Participants*

One study targeted carers of stroke survivors with aphasia³¹⁵. The remainder of the studies targeted informal carers of stroke survivors.

5.4.1.1.3 *Definition of the index condition for being a current informal carer*

Five studies^{313; 314; 316; 319; 320} did not provide any definition of the index condition for an informal carer and three studies^{63; 315; 317; 318} provide vague descriptions.

5.4.1.1.4 *Experimental interventions*

The studies included in this review are clinically diverse. Therefore it was decided that broader categories of intervention should be created to reflect the primary focus of the experimental interventions. To ensure that the process of categorisation was unbiased, each review author was asked to independently read an assign an anonymised extract describing the experimental intervention to one of three broad intervention categories. The results were collated and disagreement was resolved by consensus. The three broad types of intervention were:

- Support and information i.e., interventions that provide participants with information to connect them with necessary resources, opportunities or supports.
- Teaching procedural knowledge/ vocational education i.e., interventions that focus on preparing participants for the work of providing care to a stroke survivor and is based on manual or practical activities

- Psycho educational i.e., interventions that reinforce personal strengths, resources and coping skills of participants, in order to for example, to avoid relapse or contribute to their own health and wellness on a long-term basis.

There were six modes of delivery of intervention:

- Face to face
- Telephone
- Group - face to face
- Group - telephone
- Combination of face to face and telephone
- Internet

Four studies tested interventions aimed at providing information and support³¹⁶⁻³²⁰, three studies tested psycho education interventions³¹³⁻³¹⁵, one study tested the effects of ‘teaching procedural knowledge’⁶³. Five trials tested experimental interventions delivered face to face^{63;313;316-318;320}, two trials^{315;319} tested interventions that were delivered remotely i.e., by telephone³¹⁵ or Internet³¹⁹. One multi-arm trial³¹⁴ tested a combination of face to face and remote (telephone) delivery of the intervention. Of the six trials testing face to face experimental interventions, two were delivered to formal groups of participants^{313; 316} and the remainder were delivered on an individual basis.

5.4.1.2 Study interventions and comparisons

For details of study interventions and comparisons refer to the Characteristics of included studies table. One trial³¹⁴ compared two alternative forms of interventions against usual hospital care, comparing social problem solving therapy partnerships versus sham intervention versus usual hospital care. One trial³¹³ used a cross over design in which the participants took part in a psycho education programme, the experimental intervention, in sequence. For the purpose of this review, the end of scheduled follow-up is the end of the first treatment period at 12 weeks.

5.4.1.3 Excluded studies

For details for excluded studies with reasons see table Characteristics of excluded studies.

5.4.1.4 Risk of bias in included studies

For each included trial we extracted information about the method of randomisation and allocation concealment, blinding of outcome assessment and whether all the randomised patients were accounted for in the analysis.

5.4.1.4.1 Allocation

The inclusion criteria for this analysis required a study to be randomised. Six studies reported an adequately generated allocation sequence^{63; 313; 316-320}. Two studies^{63; 317; 318} reported adequately concealed allocation. Two studies did not conceal allocation^{313; 319}. Four studies were unclear^{314; 315; 316; 320}.

5.4.1.4.2 Blinding

It is not possible to blind key study personnel or participants in studies which do not use a placebo comparator. However, non-blinding of participants and study personnel is unlikely to introduce bias if the outcome assessment is blinded³²¹. Four studies report blinding of the outcome assessment/ assessor^{63; 313; 314; 317; 318}.

5.4.1.4.3 Incomplete outcome data

Missing continuous outcome data due to attrition is an issue across all studies. However, the extent and nature of attrition varies across trials. For details of the amount and distribution of missing outcome data, the reasons provided for missing outcome data, the investigators handling of missing data as well as the clinical context and judgement on risk of bias see table Risk of bias in included studies. Missing outcome data is likely to be associated with the outcome or perceived relevance of the intervention to the study participants.

5.4.1.4.4 Selective reporting

The majority of included studies appear to be free from suggestion of selective outcome reporting.

5.4.1.4.5 Other potential sources of bias

Two studies did not provide information on baseline characteristics^{63; 314}, there was baseline imbalance in two studies^{315; 317; 318} and insufficient information in one study to permit judgement about baseline imbalance³²⁰.

5.4.2 Effects of interventions

Overall, 1007 participants were included in this review. For details of the comparisons made for trials with outcome data, see Data and analyses. Meta-analysis of all studies across all outcomes was considered inappropriate because of the heterogeneous nature of the interventions across the included studies.

5.4.2.1 Primary outcomes

5.4.2.1.1 Informal carer stress and strain (Analysis 1.1)

5.4.2.1.1.1 Effects of 'teaching procedural knowledge' type interventions on measures of informal carer stress and strain.

One study⁶³ (n = 155 participants) assessed the effect of 'teaching procedural knowledge on informal carer stress and strain, measured by the carer strain index⁸⁹. Individual participant total scores were provided by the author. The analysis presented here is not available from the published report. The mean difference between the intervention and comparator group at the end of scheduled follow-up was -8.67 (95% confidence interval -11.30 to -6.04, p < 0.001) in favour of the 'teaching procedural knowledge' type intervention group.

5.4.2.1.1.2 Effects of 'support and information' type interventions on measures of informal carer stress and strain.

Two studies^{317; 318; 320} included support and information type interventions (n = 219 participants). One study^{317; 318} used the carer strain index⁸⁹ to measure informal carer stress and strain, another one study³²⁰ used a measure specially developed for the study. Carer stress and strain scores were available for available for 219 subjects from the two trials. The pooled result, combined as a standardized mean difference was -0.29 (95% confidence interval -0.86 to 0.27, p = 0.11), with substantial statistical heterogeneity (I² = 61%).

5.4.2.1.1.3 Effects of 'psycho educational' type interventions on measures of informal carer stress and strain.

Two studies^{313; 315} included psycho educational type interventions (n = 125 participants). One study³¹⁵ used the burden interview³²² and one³¹³ used the relatives' stress scale³²³. The pooled result combined as a standardized mean difference was 0.01 (95% CI-0.34 to 0.36, P = 0.94) showing no significant benefit for the psycho educational intervention group, with no significant heterogeneity (P = 0.50, I² = 0%).

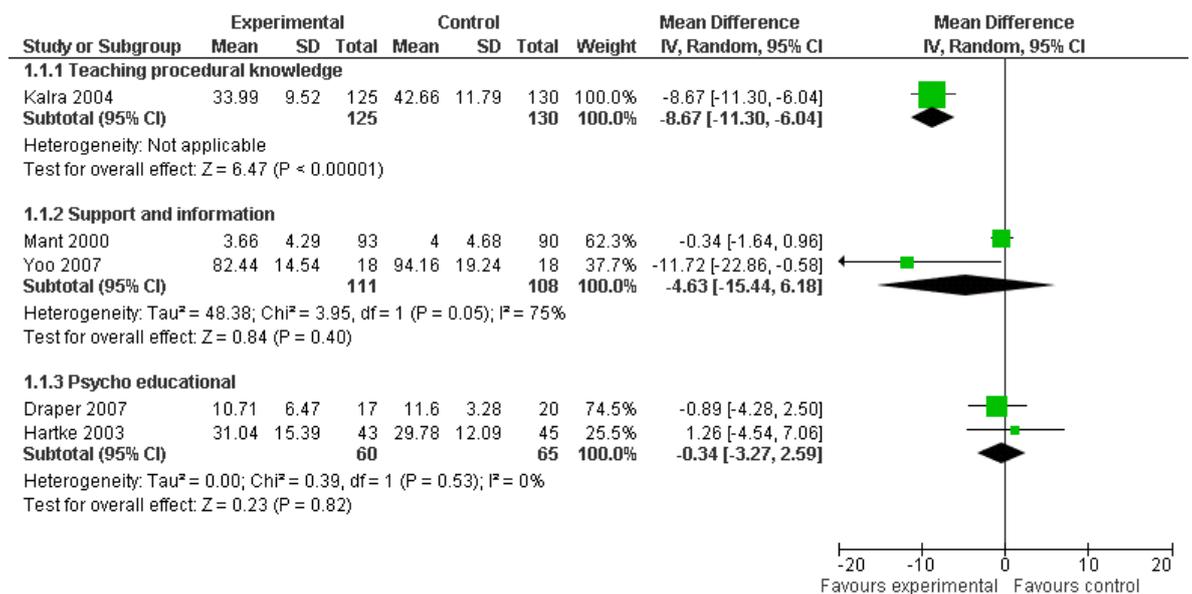


Figure 5-2 Forest plot of effects (mean difference) of interventions on measures of informal carer stress and strain. Forest plot 1.1.1 is the estimates of effect from studies investigating the effects of interventions teaching procedural knowledge. Forest plot 1.1.2 is the estimates of effect from studies investigating the effects of support and information interventions. Forest plot 1.1.3 is the estimates of effect from studies investigating the effects of support and information interventions.

Forest plot produced using the method in Revman 5.1¹⁵⁹. Illustrated is the summary data (point estimates (squares) and confidence intervals (horizontal lines through squares) for each study and a meta-analysis for each intervention subgroup (teaching procedural knowledge (1.1.1), support and information (1.1.2) and psycho educational (1.1.3) using a random effects model illustrated by a diamond. Also presented are the weights given to each study and

heterogeneity statistics (among study variance Tau^2 , χ^2 test and I^2 statistic). Meta-analysis is not possible where there is only one included study in an intervention subgroup.

5.4.2.1.2 *Informal carer well being at the end of scheduled follow up*

No study collected carer specific well being outcomes.

5.4.2.2 Secondary outcomes

5.4.2.2.1 *Global measures of stress or distress (Analysis 1.2)*

Two studies^{313; 317; 318} collected data on stress and distress using the General Health Questionnaire 28 (GHQ 28)³²⁴.

5.4.2.2.1.1 Effects of 'support and information' type interventions on global measures of stress and distress.

One study^{317; 318} (n = 183 participants) assessed the effects of an information and support intervention on informal carers' level of stress and distress. The mean difference (MD) between the 'support and information' intervention and comparator group at the end of scheduled follow-up was -0.34 (95% CI -1.64 to 0.96) P = 0.61, indicating no significant beneficial effect of the support and information intervention when compared to usual care.

5.4.2.2.1.2 Effects of 'psycho educational' type interventions on global measures of stress and distress.

One study³¹³ (n = 28 participants) assessing the effects of a psycho educational type intervention, found no significant difference between the psycho educational and wait list comparator group (MD -2.02 (95% CI -6.58 to 2.54, P = 0.39) on level of stress and distress.

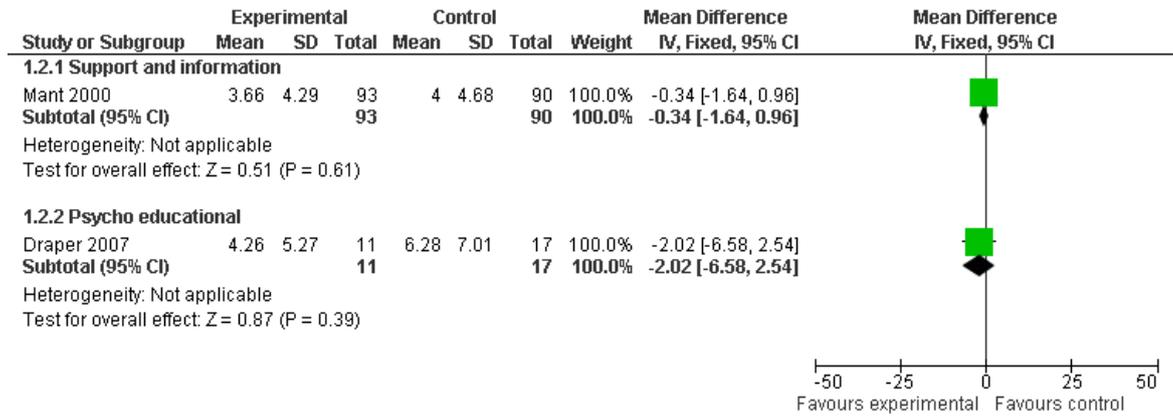


Figure 5.3 Forest plots of effects (mean difference) of interventions on measures of global measures of stress or distress. Forest plot 1.2.1 is the estimates of effect of studies investigating the effects of support and information interventions. Forest plot 1.2.2 is the estimates of effect from studies investigating the effects of support and information interventions.

Forest plot produced using the method in Revman 5.1¹⁵⁹. Illustrated is the summary data (point estimates (squares) and confidence intervals (horizontal lines through squares) for each study and a meta-analysis for each intervention subgroup (support and information (1.2.1) and psycho educational (1.2.2) using a fixed effects model illustrated by a diamond. The diamond represents the summary effect estimate however; meta-analysis was not possible because there was only one included study in each intervention subgroup.

5.4.2.2.2 Measures of anxiety (Analysis 1.3)

One study⁶³ (N = 271 participants) assessed the effects of a ‘teaching procedural knowledge’ on measures of anxiety using the Hospital Anxiety and Depression Scale (HADS)³²⁵. Individual participant total scores were provided by the author. The analysis presented here is not available from the published report. This study found no significant difference between the intervention and comparator group (risk ratio (RR) of 0.42 (0.13 to 1.29, P = 0.13)) on level of anxiety.

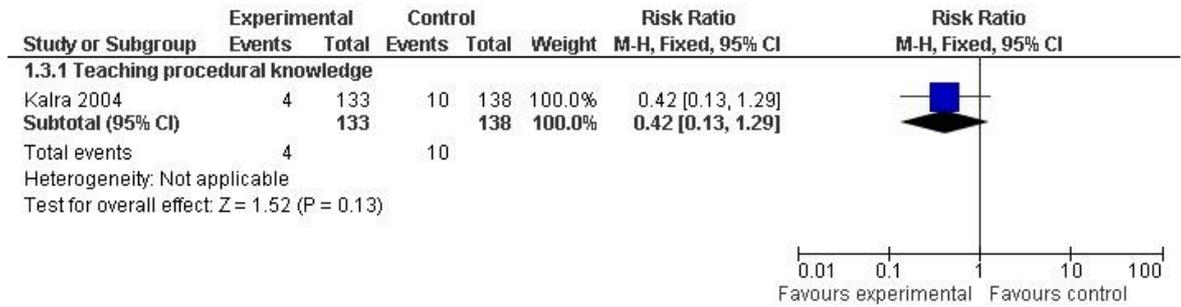


Figure 5.4 Forest plot of effects (risk ratio) of interventions on measures of measures of anxiety.

Forest plot produced using the method in Revman 5.1¹⁵⁹. Illustrated is the summary data (point estimates (squares) and confidence intervals (horizontal lines through squares)). The diamond represents the summary effect estimate however; meta-analysis was not possible because there was only one included study.

5.4.2.2.3 *Measures of depression Analysis 1.4*

Five studies collected data on measures of depression.

5.4.2.2.3.1 **Effects of ‘teaching procedural knowledge’ type interventions on measures of depression**

One study⁶³ (n = 173 participants) assessed the effect of ‘teaching procedural knowledge on measures of depression using the HADS³²⁵. Individual participant total scores were provided by the author. The analysis presented here is not available from the published report. The mean difference between the intervention and comparator group at the end of scheduled follow-up was -0.61 (95% CI -0.85 to -0.37, P < 0.001) in favour of the ‘teaching procedural knowledge’ type intervention group.

5.4.2.2.3.2 **Effects of ‘support and information’ type interventions on measures of depression**

Two studies³¹⁷⁻³¹⁹ included support and information type interventions (n = 256 participants). One study^{317; 318} used the GHQ 28¹⁵² to measure depression and one study³¹⁹ used the Centre for Epidemiologic Depression Scale (CES-D)³²⁶. The pooled result, combined as a standardized mean difference was -0.06 (95% CI -

0.31 to 0.18, $p = 0.62$), with no statistical heterogeneity ($I^2 = 0\%$), indicating no significant benefit for the ‘information and support’ intervention group.

5.4.2.2.3.3 Effects of ‘psycho educational’ type interventions on measures of depression

Two studies^{313; 314} included psycho educational type interventions ($n = 116$ participants). One study³¹³ used the GHQ 28¹⁵² and one³¹⁴ used the CES-D³²⁶. The pooled result combined as a standardized mean difference was 0.20(95% CI-0.17 to 0.57, $P = 0.28$), with substantial statistical heterogeneity ($I^2 = 55\%$) showing no significant benefit for the psycho educational intervention group.

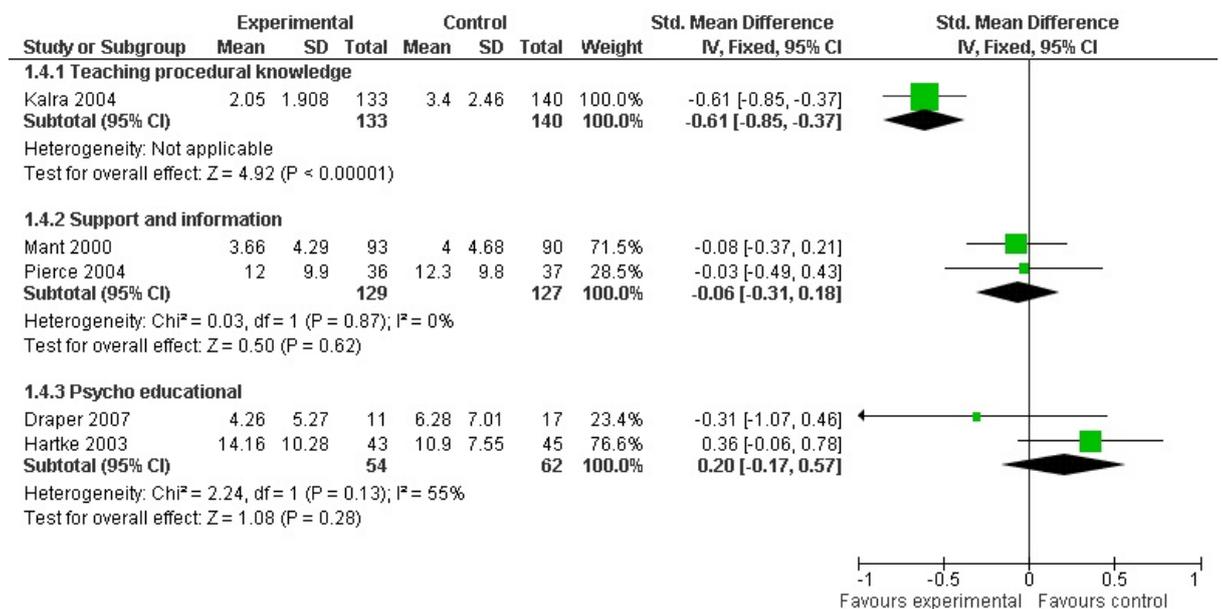


Figure 5.5 Forest plots of effects (standardised mean difference) of interventions on measures of depression. Forest plot 1.4.1 is the estimates of effect from studies investigating the effects of interventions teaching procedural knowledge. Forest plot 1.4.2 is the estimates of effect from studies investigating the effects of support and information interventions. Forest plot 1.4.3 is the estimates of effect from studies investigating the effects of support and information interventions.

Forest plot produced using the method in Revman 5.1¹⁵⁹. Illustrated is the summary data (point estimates (squares) and confidence intervals (horizontal lines through squares) for each study and a meta-analysis for each intervention subgroup (teaching procedural knowledge (1.4.1), support and information (1.4.2) and psycho educational (1.4.3) using a fixed effects model illustrated by

a diamond. Also presented are the heterogeneity statistics (among study variance τ^2 , χ^2 test and I^2 statistic). Meta-analysis is not possible when there is only one study in an intervention subgroup.

5.4.2.2.4 Measures of health related quality of life (Analysis 1.5)

Three studies^{63; 316; 317; 318} assessed health related quality of life.

5.4.2.2.4.1 Effects of 'teaching procedural knowledge' type interventions on measures of health related quality of life

One study⁶³ assessed health related quality of life (HRQOL) using the EuroQol³²⁷. This study found a significant difference in health related quality of life in favour of the experimental intervention MD - 11.97 (95% CI -15.59 to -8.35, $P < 0.001$).

5.4.2.2.4.2 Effects of 'support and information' type interventions on measures of health related quality of life

Two studies^{316; 317; 318} assessed health related quality of life (HRQOL). One study³¹⁶ assessed HRQOL using the EuroQol³²⁷ and one study^{317; 318} assessed HRQOL using the short form 36 (SF-36)³²⁸. It is not possible to pool the data from the two studies as the SF 36 measures and produces eight health domains scores, one psychometrically based physical component summary score (PCS) and one mental component summary score (MCS); not one total score.

The first study³¹⁶ showed no significant benefit for the 'information and support' group on measures of health related quality of life, MD 3.64 (95% CI -3.51 to 10.79, $P = 0.32$). The second study^{317;318} showed significant improvements in five of eight SF-36 health domains including energy and vitality, mental health, pain, physical function and general health perception in favour of the information and support group intervention (data drawn from original paper^{317;318}). The PCS and MCS scores were not available in the published paper.

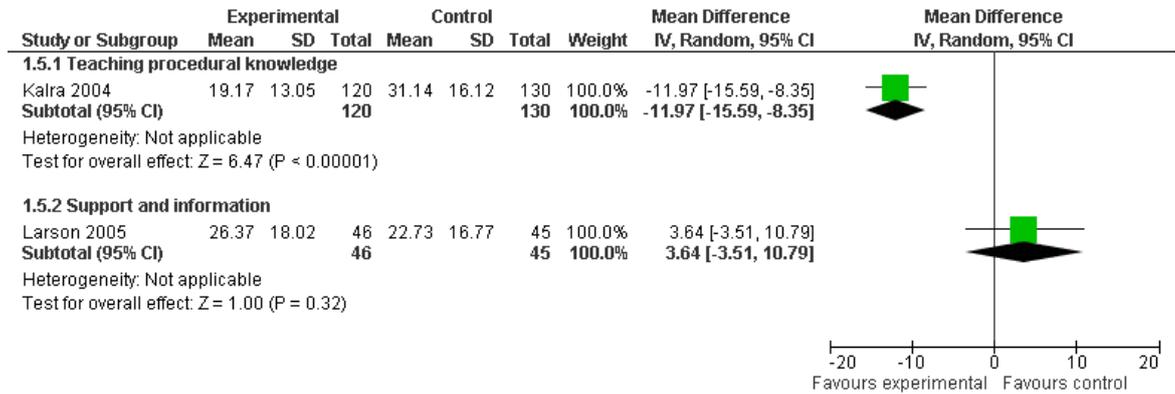


Figure 5.6 Forest plots of effects (mean difference) of interventions on measures on health related quality of life. Forest plot 1.5.1 is the estimates of effect from studies investigating the effects of interventions teaching procedural knowledge. Forest plot 1.5.2 is the estimates of effect from studies investigating the effects of support and information interventions.

Forest plot produced using the method in Revman 5.1¹⁵⁹. Illustrated is the summary data (point estimates (squares) and confidence intervals (horizontal lines through squares) for each intervention subgroup (teaching procedural knowledge (1.5.1) and support and information (1.5.2)). The diamond represents the summary effect estimate using a random effects model. Meta-analysis is not possible when there is only one study in an intervention subgroup.

5.4.2.2.5 *Informal carer satisfaction*

One study^{317; 318} assessed satisfaction with services and understanding of stroke using a carer satisfaction questionnaire³²⁹. The study reported that carers in the intervention were more satisfied with their understanding of the causes of stroke (84% vs. 72%, P = 0.04) but no more satisfied than the control group with their understanding of stroke (77% vs. 65% P = 0.06) and how to prevent another stroke (82% vs. 71%, P = 0.06). No detail was provided on satisfaction with stroke services in hospital, at discharge or after. One study³¹⁴ assessing satisfaction with health care using the client satisfaction questionnaire³³⁰ reported that carers satisfaction in the experimental and sham intervention groups remained comparable while the level of satisfaction decreased over time in the control group; no data were reported. Another study³¹⁵ assessed carer satisfaction with the characteristics of the intervention using a measure developed specifically for

that purpose, however no assessment was made comparing satisfaction in the intervention groups vs. control group.

5.4.2.2.6 *Informal carer mortality*

No study collected data on informal carer mortality.

5.5 Discussion

5.5.1 *Summary of main results*

There is currently insufficient data to support or refute the use of ‘information and support’ interventions or ‘psycho educational’ interventions for informal carers of stroke survivors to reduce or prevent carer specific stress and strain, general stress or distress, depression, anxiety or health related quality of life compared to no intervention or usual care. ‘Teaching procedural knowledge’ type interventions delivered to carers of stroke survivors prior to the stroke patients discharge from hospital, appear to reduce carer specific stress and strain, general stress or distress, depression and improve health related quality of life compared to usual care. However, this is based on data from one, small, single centre study.

5.5.2 *Overall completeness and applicability of evidence*

The goal of studies included in this review is either to evaluate a potential ‘cure’ for a health state (e.g. depression) or social state (e.g., burden) or to identify measures to prevent the sequelae of providing informal care such as stress, depression, anxiety or decline in health related quality of life.

Unlike RCTs of patients (for example stroke survivors), where subjects must have the disease in question to be admitted to trial, the participants in the included studies are free-living individuals and are not defined by the presence of disease or ill health nor are they presenting for clinical care or under active health care. A major limitation of all the included studies is lack of reporting of a detailed and precise definition of the index condition for a current informal carer making it difficult to assess fully the merits and appropriateness of the included studies. In addition, inadequate characterisation of the informal carer

study participants makes it difficult to know who the results of the study apply to and to replicate the studies in question. Moreover, an ambiguous eligibility criterion suggests a study that is not properly designed to evaluate the effects of the interventions; if a study population is chosen incorrectly then ability to detect a benefit is likely to be reduced. Furthermore, the substantial drop outs witnessed across the included studies suggests that in some instances that the intervention may not have been appropriate for the participants that were selected for enrolment in the study.

Second, 'informal carers' are perceived as individuals at high risk of adverse health outcomes. However, the effect of an individual's informal carer classification/ status on the same individual's risk of incident 'health outcomes' (including depression, anxiety, general stress and distress and health related quality of life) is not a well defined causal quantity and therefore has no obvious implications for interventions.

5.5.3 Quality of the evidence

The evidence in this review comes from eight studies from four countries carried out over the previous 12 years. The total number of participants was 1007. It is difficult to draw robust conclusions about the effects of interventions targeted towards informal carers of stroke survivors as there is a lack of a precise definition of the index condition of a current informal carer across all studies and in addition there are limitations in the study design and conduct of individual studies which raise questions about the validity of their findings.

5.5.4 Potential biases in the review process

It is believed that all the relevant randomised controlled trials have been identified. All bar one of the original authors have been successfully contacted. Any truly randomised controlled trials regardless of language of publication were sought. All papers in any language other than English have been either translated or data has been extracted from the original paper by an individual proficient in the language of the paper.

5.5.5 Agreements and disagreements with other studies or reviews

Brereton 2007³³¹ conducted a systematic review of published and unpublished research evidence of the effects of interventions for adult family carers of people who have had a stroke based on a search of seventeen electronic databases and the grey literature sources. The purpose of the review was to assess the effects of interventions targeted towards adult family carers of stroke survivors on carers' primary outcomes and to determine the conceptual basis for the intervention. Studies were limited to randomised controlled trials. The authors did review the quality of each study using the Critical Appraisal Skills Programme (CASP) tool for randomised controlled trials, with two reviewers performing double data extraction on all included studies. The review found eight trials assessing the effects of carer training interventions such as education and counselling, social problem solving partnerships, psycho educational telephone support groups, a nurse led education and support programme, as well as a support programme delivered in hospital or at home. The review found that all interventions tested in the RCTs provided some benefit. However, the authors were unable to draw conclusions because of methodological limitations.

The main differences between the Brereton systematic review and this systematic review are that the Brereton review is narrative; it focuses on a family member as the informal carer and has no a priori stated primary and secondary outcomes. In addition, there are several areas of disagreement between the Brereton review and this review around assessment of methodological quality (primarily randomisation and blinding) of the included studies that are common to both reviews^{63; 314-316}. Further, Kalra 2004⁶³ does not meet the Brereton study inclusion criteria as eligibility is not limited to family carers in either study. In addition, Van den Heuvel³³²⁻³³⁴ does not meet the criteria for a randomised controlled trial as participants were not randomly assigned to intervention and comparator groups. Evans³³⁵ is excluded from this review because it does not collect any of the outcomes of interest. However, while we disagree with certain aspects of the review methods and results, we agree with their conclusion that there is insufficient data of adequate quality to draw firm conclusions.

Eldred³³⁶ conducted a systematic review of published and unpublished research evidence of the effects of psychosocial interventions for carers of stroke survivors based on psychological principles and theoretical frameworks based on a search of eight electronic databases, hand searching, scanning reference lists and contacting experts in the field. Studies were limited to randomised controlled trials. The authors reviewed the quality of each study using a Quality Assessment Tool designed especially for the systematic review. Two reviewers independently assessed the quality of each study. No detail is provided on how data were extracted. The authors identified seven studies for inclusion. The interventions assessed included education with family counselling, education with individual counselling, individual telephone support, group telephone support, individual home visit support and group meeting support. The review found insufficient evidence to determine the effects of psychosocial interventions for informal carers of stroke survivors.

5.6 Conclusions

5.6.1 Implications for practice

There is a general acceptance that good clinical care will include providing information, advice and informal support to carers (as well as to patients). The conclusions of this review do not provide any clear evidence on how best to perform these roles.

5.6.2 Implications for research

11 studies are ongoing so a future review update is merited and may lead to firmer conclusions.

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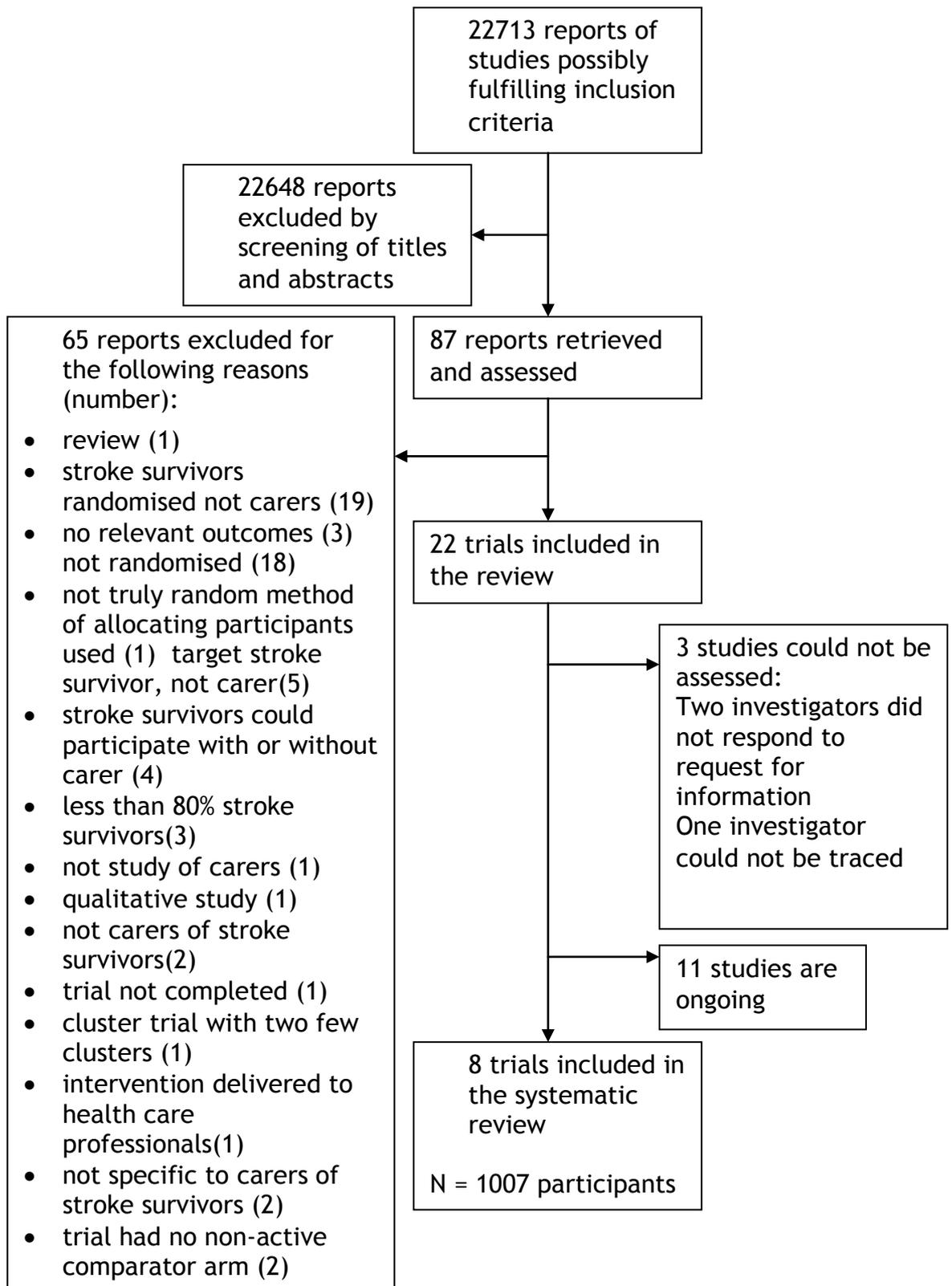


Figure 5.1 Flowchart of selection of studies for inclusion in the systematic review and meta-analysis.

Table 5- 1 Characteristics of included studies

Draper 2007 ³¹³	
Methods	Randomised controlled trial
Participants	<p>Source: Carers recruited from the rehabilitation services of three public hospitals in the Southern Eastern Sydney area health service</p> <p>Definition of carer: Not stated</p> <p>Carers inclusion criteria: Able to speak and understand sufficient English to participate in intervention and complete assessments.</p> <p>Carers exclusion criteria: None stated</p> <p>Stroke survivors inclusion criteria: A significant communication problem as assessed by the Western Aphasia battery.</p> <p>Stroke survivors exclusion criteria: None stated</p> <p>Number of carers randomised: 39 Number of carer in intervention group: 19 Number of carers in comparator group: 20</p> <p>Number of carers assessed at final follow-up: 28 Number of carers in intervention group: 17 Number of carers in comparator group: 11</p> <p>Mean age carer: mean 61.9 years % male carers: not stated</p>
Interventions	<p>Title: Psycho education programme</p> <p>Target of the intervention: carers of aphasic stroke patients</p> <p>Characteristics: Group intervention based on the SHARE programme including elements of education, psychological support and communication skills.</p> <p>Intervention provided by: Speech pathologist, social worker and clinical psychologist.</p> <p>Intervention delivered: unclear.</p> <p>Dose/frequency/ timing of intervention: one two hour group per week.</p> <p>Intervention length: four week</p> <p>Title: Wait list control</p> <p>Characteristics: Group intervention based on the SHARE programme including elements of education, psychological support and communication skills.</p> <p>Comparator intervention provided by: Speech pathologist, social worker and clinical psychologist.</p> <p>Comparator intervention delivered: unclear.</p> <p>Dose/frequency/ timing of comparator intervention: one two hour group per week.</p> <p>Comparator intervention length: four weeks.</p>
Outcomes	<p>Outcome measures: Relative's Stress Scale; General Health Questionnaire (GHQ); communication questionnaire.</p> <p>Timing of assessment: post treatment ; three month follow-up</p>

Risk of bias table

Bias	Authors Judgement	Support for judgement
Random	Low risk	<i>'Placing names into a hat and</i>

sequence generation (selection bias)		<i>drawing out one at a time...</i>
Allocation concealment (selection bias)	High risk	<i>'...and alternating between treatment or wait list control groups.'</i>
Blinding (performance bias and detection bias)	Low risk	<i>'Questionnaires sent to the homes of the paired groups.'</i>
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	High risk	Description: Selective omission of outcome from report. Judgement: Not all studies pre-specified primary outcomes have been reported.

Grant 2002 ³¹⁴	
Methods	Randomised controlled trial
Participants	<p>Source: Participants recruited from one private and one state rehabilitation facility, Birmingham, Alabama, USA</p> <p>Definition of carer: Not stated</p> <p>Carers' inclusion criteria: Age ≥ 18; related to stroke survivor by blood or marriage; responsible for providing care to stroke survivor \geq six hours per day; have sufficient use of English language to take part in telephone contacts; provided consent; contactable by telephone and lived within 100 mile radius of study centres.</p> <p>Carers' exclusion criteria: Major history of debilitating diseases such as depression, schizophrenia or alcoholism as measured by standard diagnostic criteria.</p> <p>Stroke survivors' inclusion criteria: Admitting diagnosis of Ischaemic stroke either caused by thrombi or emboli; Functional Independence Measure (FIM) score between 36 and 96; discharge destination of home.</p> <p>Stroke survivors' exclusion criteria: Major history of debilitating diseases such as depression, schizophrenia or alcoholism as measured by standard diagnostic criteria.</p> <p>Number of carers randomised: 74 Number of carer in intervention group: unclear Number of carers in comparator group A: unclear Number of carers in comparator group B: unclear</p> <p>Number of carers assessed at final follow-up: 73 Number of carers in intervention group: 26 Number of carers in comparator group A: 22 Number of carers in comparator group B: 25</p> <p>Mean age carers: 58\pm12years</p>

	% male carers: 9%
Interventions	<p>Title: Social Problem Solving Therapy Partnerships (SPTP) Characteristics: Initial three hour training provided to family carers in the home setting. Carers were taught to use a positive problem solving approach and four steps to use when solving problems. This was followed by telephone contacts. Intervention provided by: Trained nurse Intervention delivered: Home and to home by telephone. Dose/frequency/ timing of intervention: One three hour training session prior to stroke survivor being discharged. Thereafter, telephone contacts one per week for first month, one per two weeks month two and three. Intervention length: 12 weeks Co-interventions: Usual discharge planning services</p> <p>Arm 2 - Title: Sham intervention Characteristics: Telephone contacts asking about health care services stroke survivor had received since the last contact. First comparator intervention provided by: Graduate research assistant First comparator intervention delivered: To home via telephone. Dose/frequency/ timing of first comparator intervention: Telephone contacts were made one per week for first month, one per two weeks month two and three. First comparator Intervention length: 12 weeks Title: Control group Characteristics: Usual hospital care Second comparator provided by: Not applicable Second comparator delivered: Not applicable Dose/frequency/ timing of second comparator: Not applicable Second comparator length: Not applicable</p>
Outcomes	<p>Outcome measures: Medical Outcomes Study Short Form Health Survey (SF-36); Social Problem -Solving Inventory revised; The Client Satisfaction Questionnaire; Center for Epidemiologic Depression Scale (CES-D); Carer Preparedness; Caregiving Burden Scale (CBS). Timing of assessment: 13 weeks after discharge or immediately after intervention finished.</p>
Notes	Numbers of participants have been provided by Professor Joan S. Grant by email.

Risk of bias table**Bias**

Random sequence generation (selection bias)

Authors Judgement

Unclear risk

Support for judgement

'Block or restricted randomisation and choosing blocks at random to create the allocation sequence'

Allocation concealment

'The person who generated the sequence did not determine

(selection bias)		<i>eligibility and entry of patients.'</i>
Blinding (performance bias and detection bias)	Unclear risk	'Yes'
Incomplete outcome data (attrition bias)		'11 participants lost to follow-up at some point during data collection.' 11/ 74 (15%). Reason for missing data reported: yes Missing data balanced between groups: unclear Statistical methods used to deal with missing data: none Judgement: More than one outcome of interest in the report is reported incompletely and cannot be entered into the meta-analysis.
Selective reporting (reporting bias)	High risk	Selective under reporting of data.

Hartke 2003 ³¹⁵	
Methods	Randomised controlled trial
Participants	<p>Source: Participants were solicited for information through a review of stroke survivor's admission records, various media advertisements and news features and targeted community outreach. Chicago, Illinois, USA.</p> <p>Definition of carer: '...Someone who was providing emotional support in addition to participating in care in at least one of the following three areas: personal care, instrumental activities of daily living, decision making or informal case management.'</p> <p>Carers' inclusion criteria: Participating in role as carer \geqone month; aged \geq60 years; be either spouse or partner and living with stroke survivor; not actively participating in carer specific support groups; telephone in the home; sufficient hearing to allow participation in teleconference calls and outcome assessments.</p> <p>Carers' exclusion criteria: None stated</p> <p>Stroke survivors' inclusion criteria: None stated</p> <p>Stroke survivors' exclusion criteria: None stated</p> <p>Number of carers randomised: 124 Number of carer in intervention group: 68 Number of carers in comparator group: 56</p> <p>Number of carers assessed at final follow-up: 88 Number of carers in intervention group: 43 Number of carers in comparator group: 45</p> <p>Mean age carers: unclear % male carers: 24%</p>
Interventions	Title: Telephone Group Intervention

	<p>Characteristics: Psychoeducational support group delivered by telephone & group manual including audiotape of relaxation procedures and a publication on stress management.</p> <p>Intervention provided by: Clinicians with a psychology, social work or nursing background.</p> <p>Intervention delivered: Home setting via telephone</p> <p>Dose/frequency/ timing of intervention: eight one hour session</p> <p>Intervention length: Not applicable</p> <p>Co-interventions: None stated</p> <p>Title: Control condition</p> <p>Characteristics: A publication on stress management and a brief description of carers stress and stroke</p> <p>First comparator provided by: Not applicable</p> <p>First comparator delivered: Not applicable</p> <p>Dose/frequency/ timing of first comparator: NA</p>
Outcomes	<p>Outcome measures: Center for Epidemiologic Depression Scale (CES-D); UCLA Loneliness Scale; The Carer Competence Scale; The Burden Interview (BI); The pressing Problem Index.</p> <p>Timing of assessment: Immediately after support group; and, six months after enrolling in study.</p>

Risk of bias table

Bias	Authors Judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<i>'Participants were then randomly assigned to a usual care or telephone support group condition and were followed-up for 6 months to test the enduring effects of the intervention.'</i>
Allocation concealment (selection bias)	Unclear risk	<i>'Participants were then randomly assigned to a usual care or telephone support group condition and were followed-up for 6 months to test the enduring effects of the intervention.'</i>
Blinding (performance bias and detection bias)	Unclear risk	All assessments were conducted by members of the research staff via individual telephone interviews.'
Incomplete outcome data (attrition bias)	High risk	<p>Description: 25/68 (37%) participants in treatment arm lost to follow-up and 11/56 (20%) participants in the comparator group lost to follow-up.</p> <p>Reason for missing data reported: yes, but not in sufficient detail. 'the most frequent reason for dropping out of control group was difficulty scheduling appointments, whereas the most frequent reasons for dropping out of the treatment group were death of spouse or perception of lack of need for intervention.'</p> <p>Missing data balanced between groups: No</p> <p>Statistical methods used to deal with missing data: None</p>

<p>Selective reporting (reporting bias)</p>	<p>Judgement: difference in means among missing outcomes enough to induce clinically relevant bias in observed effect size.</p> <p>Low risk</p> <p>All studies pre-specified outcomes have been reported</p>
<p>Kalra 2004⁶³</p>	
<p>Methods</p>	<p>Procedures for enrolling a participant and allocating the treatment (allocation concealment procedures):</p> <p>Methods used to generate the sequence in which participants will be randomised (sequence generation):</p> <p>Procedures for preventing knowledge of the allocated intervention:</p> <p>Who is/are masked/blinded:</p>
<p>Participants</p>	<p>Source: Stroke patients admitted to a stroke rehabilitation unit, London, UK.</p> <p>Definition of carer: The main person (other than health, social, or voluntary care provider) helping with activities of daily living and advocating on behalf of the stroke survivors.</p> <p>Carers' inclusion criteria: No notable disability; Rankin score 0 to two; willing to participate.</p> <p>Carers' exclusion criteria: None stated</p> <p>Stroke survivors' inclusion criteria: Independent in activities of daily living prior to stroke onset; medically and neurologically stable; expected to return home with residual disability.</p> <p>Number of stroke patients and carers randomised as a dyad: 300</p> <p> Number of carer in intervention group: 151</p> <p> Number of carers in comparator group: 149</p> <p>Number of stroke patients and carers assessed at final follow-up as a dyad: 268</p> <p> Number of carers in intervention group: 134</p> <p> Number of carers in comparator group: 134</p> <p>Stroke survivors exclusion criteria: NA</p> <p>Mean age carers: unclear</p> <p>% male carers: unclear</p>
<p>Interventions</p>	<p>Title: Care giver training</p> <p>Characteristics: Formal training of carers in the prevention and management of common problems after stroke including: Instruction on: management of pressure sores and prevention of bed sores; continence; positioning; nutrition; gait facilitation, and 'hands on' training in: lifting and handling techniques; mobility and transfers; assistance with activities of daily living and communication. All tailored towards individual patients. A formal follow-up session was provided when the stroke survivor had returned home.</p> <p>Intervention provided by: members of the multidisciplinary team as appropriate.</p> <p>Intervention delivered: in stroke rehabilitation unit.</p> <p>Dose/frequency/ timing of intervention: Three to five sessions depending on need. Each session lasted 30-45</p>

	<p>minutes. Training commenced when patient was considered suitable for discharge.</p> <p>Intervention length: Not applicable</p> <p>Title: Conventional hospital care</p> <p>Characteristics: Conventional care was provided according to existing guidelines. Conventional care consisted: of information on stroke; encouragement to attend nursing and allied health professional sessions to gain information on for example facilitating transfers; and, advice on community services, benefits, support services organised and run by voluntary organisations.</p> <p>First comparator provided by: Multidisciplinary team</p> <p>First comparator delivered: in stroke rehabilitation unit</p> <p>Dose/frequency/ timing of first comparator: Not applicable</p> <p>First comparator length: Not applicable</p>
Outcomes	<p>Outcome measures: Frenchay activities index; Hospital Anxiety and Depression Scale; Carer burden scale; Euroqol.</p> <p>Timing of assessment: Three months, 12 months.</p>

Risk of bias table

Bias	Authors Judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<i>'We used computer generated random numbers to prepare the allocation schedule in advance.'</i>
Allocation concealment (selection bias)	Low risk	<i>'After baseline assessment the responsible assessor telephoned the randomisation office with patients' identification details only. A clerical worker entered these details on a computer database in strict referral order and was given a patient allocation, which was relayed to the assessor.'</i>
Blinding (performance bias and detection bias)	Low risk	<i>'An observer who did not participate in allocation or management of patients assessed outcome at three and 12 months after stroke onset.'</i>
Incomplete outcome data (attrition bias)	Unclear	<p>Description: 17/151 (11%) outcome data missing for participants in the experimental group and 15/149 (10%) outcome data missing from participants in the comparator group at the end of scheduled follow-up.</p> <p>Reason for missing data reported: <i>'...communication problems, perceived lack of relevance, lack of time, fatigue, or disinclination in patients and carers...'</i></p> <p>Although unclear if information refers to active intervention or usual care group.</p> <p>Missing data balanced between groups:</p>

unclear

Statistical methods used to deal with missing data: None. Only completed assessments were included at each time point. However, sensitivity analyses were performed to examine the effects of missing values for carer burden and health related quality of life outcomes.

Judgement: Insufficient reporting of reasons for missing data across interventions groups to permit judgement
All studies pre-specified outcomes have been reported.

Selective reporting (reporting bias)

Low risk

Larson 2005 ³¹⁶	
Methods	Randomised controlled trial
Participants	<p>Source: The spouses of stroke survivors admitted to the stroke unit at Danderyd University Hospital, Stockholm, Sweden, between November 2000 and July 2002.</p> <p>Definition of carer: Not stated</p> <p>Carers' inclusion criteria: None stated</p> <p>Carers' exclusion criteria: If it was not possible to obtain information from the spouse</p> <p>Stroke survivors' inclusion criteria: None stated</p> <p>Stroke survivors' exclusion criteria: The stroke survivor was not going to return home after discharge</p> <p>Number of carers randomised: 100 Number of carer in intervention group: 50 Number of carers in comparator group: 50</p> <p>Number of carers assessed at final follow-up: 91 Number of carers in intervention group: 46 Number of carers in comparator group: 45</p> <p>Mean age carers: 67</p> <p>% male carers: 20%</p>
Interventions	<p>Title: Nurse led support and education programme</p> <p>Characteristics: Education programme, delivered to groups of ten carers. Topics covered included: the nature of stroke, treatment and recovery, psychological and social effects of stroke and prevention of further stroke. Participants were free to contact the stroke nurse specialist if and when required.</p> <p>Intervention provided by: stroke nurse specialist</p> <p>Intervention delivered: hospital setting</p> <p>Dose/frequency/ timing of intervention: six sessions over a period of six months</p> <p>Intervention length: six months</p> <p>Title: Control</p> <p>Characteristics: Routine information during stroke survivor's stay in hospital and at discharge. A 1.5 hour open session provided by a stroke specialist physician was also available for control group to attend should they wish.</p> <p>First comparator intervention provided by: stroke physician</p>

	First comparator Intervention delivered: In hospital Dose/frequency/ timing of first comparator intervention: NA
Outcomes	QOL; Bradley's well-being questionnaire; Life Situation among Spouses after the Stroke event (LISS) questionnaire; Euroqol. Timing of assessment: six months; 12 months

Risk of bias table

Bias	Authors Judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<i>'The investigator place the envelopes on the table in front of the participant, who chose one envelope from the packet, thus the number of envelopes diminished with each new participant.'</i>
Allocation concealment (selection bias)	Unclear risk	<i>'The randomisation was performed in blocks of 20, 10 in each arm. Sealed envelopes. With a note intervention group/control group. Were prepared before the meeting with the participant in each block.'</i> <i>'The investigator place the envelopes on the table in front of the participant, who chose one envelope from the packet, thus the number of envelopes diminished with each new participant.'</i>
Blinding (performance bias and detection bias)	Low risk	<i>'Outcomes were assessed by self-rated questionnaires.'</i>
Incomplete outcome data (attrition bias)	Low risk	4/ 50 (8%) drop outs in the intervention group after randomisation and 5/50 (10%) drop outs in comparator group. Reason for missing data reported: Not reported Missing data balanced between groups: Yes. Statistical methods used to deal with missing data: None reported. Judgement: Reasons for missing data unlikely to be related to true outcome.
Selective reporting (reporting bias)	Low risk	All studies pre-specified outcomes have been reported.

Mant 2000^{317;318}

Methods	Randomised controlled trial
Participants	Source: Any patient admitted with acute stroke (first or recurrent) to hospitals in Oxford between August 1995 and February 1998, identified from a hospital based stroke register. Definition of carer: The person (other than a health care professional) perceived by the patient or family as normally being most responsible for day-to-day decision making and provision of care.

	<p>Carers' inclusion criteria: None stated</p> <p>Carers' exclusion criteria: None stated</p> <p>Stroke survivors' inclusion criteria: Aged ≥ 18; resident in Oxfordshire; had a close family carer.</p> <p>Stroke survivors' exclusion criteria: Admitted to hospital from a nursing home; participating in another trial; identified for inclusion > 6 weeks after stroke or hospital discharge; main medical problem not stroke.</p> <p>Number of stroke patients and carers randomised as a dyad: 520</p> <p>Number of carer in intervention group: 258</p> <p>Number of carers in comparator group: 262</p> <p>Number of carers assessed at final follow-up: 267</p> <p>Number of carers in intervention group: 130</p> <p>Number of carers in comparator group: 137</p> <p>Number of stroke survivors assessed at final follow-up: 323</p> <p>Number of stroke patients in intervention group: 156</p> <p>Number of stroke patients in comparator group: 167</p> <p>Mean age carers: 64.4 years</p> <p>% male carers: 32.6%</p>
Interventions	<p>Title: Family support</p> <p>Characteristics: Dependent on the problems, needs and requests of families.</p> <p>Intervention provided by: Family support organiser (FSO).</p> <p>Intervention delivered: Not stated.</p> <p>Dose/frequency/ timing of intervention: At the discretion of the FSO.</p> <p>Intervention length: Variable.</p> <p>Title: Normal care</p> <p>Characteristics: Normal care</p> <p>Intervention provided by: Not applicable</p> <p>Intervention delivered: Not applicable</p> <p>Dose/frequency/ timing of intervention: Not applicable</p>
Outcomes	<p>Frenchay activities Index; General Health Questionnaire 28; Carer strain index; Dartmouth co-op charts; knowledge about stroke and use of services.</p> <p>Timing of assessment: six months.</p>

Risk of bias table

Bias	Authors Judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<i>'Randomisation was ...prepared from computer generated random numbers.'</i>
Allocation concealment (selection bias)	Low risk	<i>'Randomisation was done by staff not involved in the care of patients, by use of sequentially numbered (opaque sealed) envelopes in blocks of ten.'</i>
Blinding (performance bias and detection bias)	Low risk	<i>'Follow-up visits were done, 6 months after stroke, at families' homes by a researcher who was unaware of the</i>

Incomplete outcome data (attrition bias)	Unclear	<p><i>intervention group status.'</i></p> <p>128/258(50%) outcome data missing for participants in the experimental group and 125/262 (48%) outcome data missing from participants in the comparator group at the end of scheduled follow-up for the primary outcome (carer stress or strain).</p> <p>Reason for missing data reported: Not reported</p> <p>Missing data balanced between groups: Yes.</p> <p>Statistical methods used to deal with missing data: None reported.</p> <p>Judgement: Insufficient reporting of attrition to permit judgement i.e. no reasons for missing data provided</p>
Selective reporting (reporting bias)	Low risk	The majority of pre-specified outcomes have been reported.
Pierce 2004 ³¹⁹		
Methods	Randomised controlled trial	
Participants	<p>Source: Participants were first time stroke survivors recruited from four rehabilitation centres and discharged home to one of two Midwestern states, USA during the period May 2002 to December 2004.</p> <p>Definition of carer: Not stated</p> <p>Carers' inclusion criteria: age ≥ 21 years; person responsible for providing day to day care for stroke survivor; must be able to read, write and understand English; must have a telephone and television to facilitate MSN TV and Internet access.</p> <p>Carers' exclusion criteria: None stated</p> <p>Stroke survivors' inclusion criteria: Being discharged to home in the northern Ohio or southern Michigan areas.</p> <p>Stroke survivors' exclusion criteria: Not applicable</p> <p>Number of carers randomised: 103</p> <p>Number of carer in intervention group: 51</p> <p>Number of carers in comparator group: 52</p> <p>Number of carers assessed at final follow-up: 73</p> <p>Number of carers in intervention group: 36</p> <p>Number of carers in comparator group: 37</p> <p>Mean age carers: Not stated</p> <p>% male carers: 24.7%</p>	
Interventions	<p>Title: Caring-Web</p> <p>Characteristics: Web-based education and support in the home setting. The web-based support consisted of: 1) linked web sites about stroke and caring 2) customised educational information or tips specific to carers needs 3) an email forum with access to a nurse specialist and multidisciplinary for advice or information 4) facilitation of non structured email</p>	

	<p>discussion.</p> <p>Intervention provided by: Not applicable</p> <p>Intervention delivered: via the Internet to the home setting</p> <p>Dose/frequency/ timing of intervention: NA</p> <p>Intervention length: One year.</p> <p>Co-intervention: unclear</p> <p>Title: non-Web user group.</p> <p>Characteristics: Unclear</p> <p>Intervention provided by: Unclear</p> <p>Intervention delivered: Unclear</p> <p>Dose/frequency/ timing of intervention: Unclear</p>
Outcomes	<p>Centre for Epidemiological studies depression scale (CES-D); Satisfaction with life scale (SWLS); Survivors' health care service use.</p> <p>Timing of assessment: every 3 months. Stroke survivors' health service use, every two weeks.</p>

Risk of bias table

Bias	Authors Judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<i>'A block randomisation list with four blocks of equal sizes was generated using a SAS code.'</i>
Allocation concealment (selection bias)	High risk	<i>'There was no concealed allocation, it was not blind.'</i>
Blinding (performance bias and detection bias)	High risk	<i>'No, in this study the interviewers knew who was in web or non-web group, as the questionnaire asked if the subject had problems using the Internet and the web-based equipment and control group, as the questionnaire. The study coordinator was not blinded to the allocation. The investigators were blinded to allocation.'</i>
Incomplete outcome data (attrition bias)	High risk	<p>9/51 (18%) participants in the experimental group and 12/52 (23%) in the comparator group were lost to follow-up. A further 6/51 (12%) participants in the experimental group and 3/52 (6%) participants comparator group were expelled from trial because of lack of adherence.</p> <p>Reason for missing data: includes immediate drop out following assignment, death of care recipient, transfer of care recipient to nursing home care, dissolution of care receiver/ care recipient partnership, carer</p>

illness, change of address, drop out due to time constraints.

Statistical methods used to deal with missing data: None reported.

Judgement: Imbalance in numbers and reasons for missing data across intervention groups, particularly in relation to refusal to participate post randomisation and the need for expulsions.

Selective reporting (reporting bias)

Low risk

All studies pre-specified outcomes have been reported.

Yoo 2007 ³²⁰	
Methods	Randomised controlled trial
Participants	<p>Source: Carers (all of whom were family members) of stroke patients admitted to a neurosurgery ward of a university hospital, Seoul, Korea.</p> <p>Definition of carer: Not stated</p> <p>Carers' inclusion criteria: Unclear</p> <p>Carers' exclusion criteria: Unclear</p> <p>Stroke survivors' inclusion criteria: Unclear</p> <p>Stroke survivors' exclusion criteria: Unclear</p> <p>Number of carers randomised: 36</p> <p> Number of carer in intervention group: 18</p> <p> Number of carers in comparator group: 18</p> <p>Number of carers assessed at final follow-up:</p> <p> Number of carers in intervention group: 18</p> <p> Number of carers in comparator group: 18</p> <p>Mean age carers: Unclear</p> <p>% male carers: Unclear</p>
Interventions	<p>Title: Support group intervention</p> <p>Characteristics: Unclear</p> <p>Intervention provided by: nurses</p> <p>Intervention delivered: Hospital</p> <p>Dose/frequency/ timing of intervention: six times, three times per week, each group lasted 50 minutes</p> <p>Intervention length: two weeks</p> <p>Title: No treatment</p> <p>Characteristics: Not applicable</p> <p>Intervention provided by: Not applicable</p> <p>Intervention delivered: Not applicable</p> <p>Dose/frequency/ timing of intervention: Not applicable</p>
Outcomes	Burden questionnaire developed specifically for the purpose of the study.

Risk of bias table

Bias

Authors

Support for judgement

Judgement

Random sequence generation (selection bias)

Unclear risk

Not available

Allocation concealment (selection

Unclear risk

Not available

bias)

Blinding (performance
bias and detection bias

Unclear risk

Not available

Incomplete outcome
data (attrition bias)

Unclear risk

Not available

Selective reporting
(reporting bias)

Unclear risk

Not available

Table 5-2 Characteristics of excluded studies

Name of study	Reason for exclusion
Albert 2002 ³³⁷	Not randomised.
Bakas 2005 ³³⁸	No non-active comparator arm.
Bhakta 2000 ³³⁹	Targets stroke survivors, not carers.
Bhogal 2003 ³⁴⁰	Systematic review.
Bjorkdhal 2007 ³⁴¹	Sub (non randomised) study nested within a larger randomised controlled trial
Boter 2004 ³⁴²	Stroke survivors randomised, not carers
Burton 2005 ³⁴³	Stroke survivors randomised, not carers.
Carnavale 2006 ³⁴⁴	Less than 80% stroke patients.
Chang 2000 ³⁴⁵	Targeted towards stroke survivors not carers.
Choi 2006 ³⁴⁶	Not a 'truly' randomised RCT and study does not include outcomes relevant to the review.
Clark 2006 ³⁴⁷	Focused on 'families' of stroke survivors, not carers or caring.
Dennis 1997 ³⁴⁸	Stroke survivors randomised, not carers.
Dickens 2005 ³⁴⁹	Stroke survivors randomised, not carers.
Evans 1988 ^{350;351}	Study does not collect outcomes relevant to the review.
Forster 1996 ³⁵²	Stroke survivors randomised, not carers.
Forster 1999 ³⁵³⁻³⁵⁵	Stroke survivors randomised, not carers.
Forster 2005 ^{356;357}	Stroke survivors randomised, not carers.
Glass 2000 ^{358;360}	Stroke survivors randomised, not carers.
Grant 1999 ³⁶¹	No non-active comparator arm
Gräsel 2004 ³⁶²⁻³⁶⁴	Controlled trial, not an RCT.
Gu 1998 ³⁶⁵	Stroke survivors and carers were not recruited as a dyad.
Heier 1999 ³⁶⁶	Not a 'truly' randomised RCT.
Hoffman 2003 ³⁶⁷⁻³⁶⁹	Stroke survivors included if they had no identifiable carers, therefore stroke survivors and carer not randomised as a dyad.
Huo 2006 ³⁷⁰	Not RCT
Johnston 2007 ³⁷¹	Stroke survivors randomised, not carers.
King 2007 ³⁷²	Qualitative study
Kuo 2005 ³⁷³	Not RCT
Lee 2005 ³⁷⁴	Not RCT
Lincoln 2003 ³⁷⁵	Stroke survivors included if they had no

	identifiable carer, therefore stroke survivors and carer not randomised as a dyad.
Lincoln 2004 ³⁷⁶	Stroke survivors randomised, not carers.
Louie 2006 ³⁷⁷	Not RCT
Low 2000 ³⁶⁸⁻³⁷⁹	Stroke survivors randomised, not carers.
Lowe ³⁸⁰	Not RCT
Mant 1998 ³⁸¹	Stroke survivors randomised, not carers
Marsden 2009 ³⁸²	Stroke survivors included if their carer was participating or not, therefore stroke survivors and carer not randomised as a dyad.
Marziali 2005 ³⁸³	Not RCT
Mayo 2000 ³⁸⁴	Stroke survivors randomised, not carers.
McBride 2004 ³⁸⁵	Stroke survivors randomised, not carers.
McEwen 2005 ³⁸⁶	Intervention delivered to health care professionals.
McLellan 1995 ³⁸⁷⁻³⁸⁹	Stroke survivors not carers were randomised not patients and carers as a dyad.
Meng 2000 ³⁹⁰	Stroke survivors recruited, not carers.
Mennemeyer 2006 ³⁹¹	Not RCT
Moroni 2007 ³⁹²	Not RCT
Napolitan 1999 ³⁹³	Not RCT
Oupra 2010 ³⁹⁴	Not randomised
Overs 1971 ³⁹⁵	Intervention focused on stroke survivors, not carers.
Pain 1990 ³⁹⁶	Stroke survivors randomised, not carers.
Pfeiffer 2008 ³⁹⁷	Not RCT
Printz-Feddersen 1990 ³⁹⁸	Not RCT.
Randomski 2007 ³⁹⁹	Intervention focused on stroke survivors, not carers.
Rivera 2008 ⁴⁰⁰	Not carers of stroke survivors.
Rodgers 1999 ⁴⁰¹	Stroke survivors could participate without carers.
Ryynannen 2007 ^{402; 403}	< 80% stroke survivors.
Shyu 2008 ⁴⁰⁴	Cluster trial with very small number of clusters (N = 4)
Stewart 2006 ⁴⁰⁵	Not RCT.
Tilling 2005 ⁴⁰⁶	Stroke survivors randomised, not carers.
Tran 2004 ⁴⁰⁷	Not RCT.
Van den Heuvel 2000 ⁴⁰⁸⁻⁴¹⁰	Not randomised.
Van Puymbroeck 2007 ⁴¹¹	Not stroke.

Wilz 2007 ⁴¹²	Not a randomised controlled trial.
Wilz 2008 ⁴¹³	No carer-related outcomes.
Wolff 2009 ⁴¹⁴	Not stroke specific.
Yankovskaya 2004 ⁴¹⁵⁻⁴¹⁷	Not RCT.
Young 2007 ⁴¹⁸	Trial abandoned.
Zimmer 1985 ⁴¹⁹	Less than 80% stroke survivors & carers included.

Table 5-3 Table of ongoing studies

Bakas 2010⁴²⁰

Study name	Telephone Assessment and Skill-Building Kit for Stroke Carers
Methods	Randomised controlled trial
Participants	No further information available at present
Interventions	Telephone Assessment and Skill-Building Kit
Outcomes	No further information available at present
Starting date	2010
Contact information	Professor Tamilyn Bakas, School of Nursing, Indiana University, USA. Tel: (317) 274-4695 Nursing 417 Email: tbakas@iupui.edu

Cameron 2009⁴²¹

Study name	Optimizing Stroke Family Carer Support Across the Care Continuum by Improving the Timing of Intervention Delivery
Methods	Multi-province randomised controlled trial Study design: Interventional Study type: Allocation: Randomised Endpoint Classification: Efficacy Study Intervention Model: Parallel Assignment Masking: Open Label Primary Purpose: Supportive Care
Participants	Inclusion Criteria: Participants must speak and read English and be the primary family caregiver of a person who is receiving care for their first hospitalization for an ischemic or hemorrhagic stroke and whose anticipated ultimate destination after discharge is a private residence or apartment building. Stroke survivors must exhibit at least minimal disability (i.e., are referred to at least one rehabilitation health care professional during acute care). They may be admitted to short or long-duration inpatient (maximum duration of 6 months) or outpatient rehabilitation or return directly home. Exclusion Criteria: Caregivers of terminally ill stroke survivors or of survivors discharged to complex continuing care, long-term care or assisted retirement residences.
Interventions	Self-directed program versus Timing it Right (TIR) Stroke Family Support Person Intervention versus no intervention
Outcomes	Primary outcome. Carer's perceived social support,

	<p>assessed using the Medical Outcomes Study Social Support Scale</p> <p>Secondary outcomes. Mental health assessed by the Positive Affect Scale and Centre for Epidemiological Studies Depression Scale.</p> <p>Carers' participation in valued activities assessed by the Caregiving Impact Scale.</p> <p>Data will be collected at baseline, 3, 6 and 12-months post-stroke</p>
Starting date	September 2009
Contact information	<p>Jill Cameron (Assistant Professor) Department of Occupational Science and Occupational Therapy</p> <p>Tel: 416-978-2041</p> <p>Email: jill.cameron@utoronto.ca</p>

Díez 2008⁴²²

Study name	Carers workshop impact in severe stroke patients
Methods	Randomized controlled trial
Participants	Carer between 18-80 years old; informed consent signature (signed by the carer); must be free from invalidant disease or two chronic diseases or one mental disease or history of psychiatric problems, stroke survivor must have a discharge mRS of ≥ 2 points.
Interventions	Carers' workshop versus classical discharge information (i.e., information booklet pr-discharge talk from nurse).
Outcomes	Anxiety, stress and depression.
Starting date	2008
Contact information	<p>Dr. Sergio Illanes Díez</p> <p>Departamento de Neurología/Neurocirugía, Santos Dumont 999, sector E. Independencia, Santiago. Chile.</p> <p>Email: Sergio.illanes@gmail.com</p>
Notes	Carers' workshops versus regular carers' information. Outcomes, studying carer's anxiety, stress and depression. Hospital Clínico Universidad de Chile. Santiago, Chile

Eames 2010⁴²³

Study name	Eames 2010
Methods	<p>Procedures for enrolling a participant and allocating the treatment (allocation concealment procedures):</p> <p>Methods used to generate the sequence in which participants will be randomised (sequence generation):</p> <p>Procedures for preventing knowledge of the allocated intervention:</p> <p>Who is/are masked/blinded:</p>
Participants	<p>Inclusion criteria: Patients or carers of patients - with a current admission for stroke (first of subsequent), who are medically stable with good prognosis and aged 18 or over.</p> <p>Exclusion criteria:</p>

	<p>Residence in residential care facility prior to admission, or have residential care as a planned discharge destination. Unable to provide informed consent or complete assessments due to inadequate English, cognitive, communication, visual or hearing problems. Carers are eligible to participate even if the stroke survivor meets the exclusion criteria.</p>
Interventions	<p>1. Intervention The education and support package consists of a written education booklet that provides tailored information, supplemented by verbal reinforcement and repetition of the information contained therein stroke. This verbal reinforcement will occur both face-to-face (prior to hospital discharge) and over the telephone (after hospital discharge) for up to 3 months post-discharge.</p> <p>The written education booklet contains topics including the definition, causes, warning signs, risk factors, effects, diagnosis and treatment of stroke, as well as rehabilitation, recovery, returning to activities, going home, practical management strategies and services and support available after stroke.</p> <p>Face-to-face contact will be made up to three times with intervention participants, each contact estimated to last between 5 and 20 minutes.</p> <p>Telephone support will be initiated up to three times over the first 3 months post discharge, with each call estimated to last between 2 and 10 minutes. Additionally, over this time period, intervention participants will have the option to call to ask questions, again same time period.</p> <p>Comparator Standard care: the usual contact that clients and their carers/family members would receive from the hospital's treating team members. This would include medical assessment and treatment, nursing care, assessment and/or treatment from allied health staff, discharge planning and any information or education associated with this treatment. The control group will receive no information or intervention from the principal researcher.</p>
Outcomes	<p>Primary outcome: Stroke-related knowledge as determined by a stroke knowledge questionnaire.</p> <p>Secondary outcomes:</p> <ol style="list-style-type: none"> 1. Stroke-risk factor awareness. 2. Self-efficacy. 3. Stroke risk-related behaviour change and readiness to change these behaviours. 4. Anxiety and depression (Hospital Anxiety and Depression Scale). 5. Client quality of life and carer burden (using the Carer Strain Index).

	6. Satisfaction.
Starting date	1/09/2008
Contact information	Sally Eames PhD Candidate Division of Occupational Therapy School of Health and Rehabilitation Sciences Services Road The University of Queensland St Lucia, QLD 4072 Tel: + 61 7 3365 2870 Email: s.eames@uq.edu.au
Notes	ACTRN12608000469314 and the link is: http://www.anzctr.org.au/trial_view.aspx?ID=83109

Forster 2007⁴²⁴

Study name	Training Carers after Stroke (TRACS): a cluster randomised controlled trial of a structured training programme for carers of in-patients after stroke
Methods	Pragmatic multicentre cluster randomised controlled trial with blinded follow-up
Participants	<p>Inclusion criteria</p> <p>Stroke Rehabilitation Units: A stroke rehabilitation unit will be defined according to the definition provided by the Royal College of Physicians of London for the National Sentinel Stroke Audit 2004 by the presence of 4/5 of the following criteria:</p> <ol style="list-style-type: none"> 1. Consultant physician with responsibility for stroke 2. Formal links with patient and carer organisations 3. Multidisciplinary meetings at least weekly to plan patient care 4. Provision of information to patients about stroke 5. Continuing education programmes for staff <p>Patient:</p> <ol style="list-style-type: none"> 1. Primary diagnosis of new stroke 2. Medically stable (defined as sitting out of bed for at least four hours per day) 3. Likely discharge destination home or home but with residual disability (defined as a modified Rankin score of ≥ 3) 4. Have a carer available, defined as the main person, other than health, social, or voluntary care provider, helping with activities of daily living and advocating on behalf of the patient, who has no notable disability (defined as a modified Rankin score of 0-2) and who is willing and able to provide support after discharge. 5. Written informed patient consent/relative assent and carer consent will be obtained prior to any trial specific procedures <p>Carer:</p> <ol style="list-style-type: none"> 1. Carer is willing and able to provide support after discharge 2. Fulfils the trial definition of a carer

	<p>1. If discharge is planned within one week of admission to the stroke rehabilitation unit (insufficient time to instigate the intervention)</p> <p>2. If the patient is in need of palliative care</p> <p>3. If the patient or carer were registered to the trial on a previous admission</p> <p>Exclusion criteria</p> <p>1. If discharge is planned within one week of admission to the stroke rehabilitation unit (insufficient time to instigate the intervention)</p> <p>2. If the patient is in need of palliative care</p> <p>3. If the patient or carer were registered to the trial on a previous admission</p>
Interventions	<p>This is a cluster, randomised, controlled trial and aims to recruit 900 patients and carers in 36 stroke rehabilitation units. The intervention developed by Kalra and colleagues is known as the London Stroke Carer Training Course (LSCTC) and comprises a number of carer training sessions, competency assessment and one follow up session after discharge. The multidisciplinary teams (MDTs) in the units randomised to the intervention group will be trained to deliver the LSCTC, whilst those randomised to the control group will continue to provide usual care as per the National Guidelines.</p> <p>Stroke rehabilitation units randomised to the control group will continue to provide usual care as per the National Guidelines for Stroke.</p>
Outcomes	<p>Current secondary outcome measure(s) as of 19/03/2008:</p> <p>Patient:</p> <ol style="list-style-type: none"> 1. Hospital Anxiety and Depression Scale (HADS) (mood) 2. Euro-quality of life (EQ-5D) (health state) 3. Barthel Index (activities of daily living) 4. Death 5. Institutionalisation 6. Re-admission 7. Stroke Impact Scale (functional ability and health related quality of life) 8. Costs based on Client Service Receipt Inventory <p>Carer:</p> <ol style="list-style-type: none"> 1. Compliance with intervention 2. Frenchay activities index (social restriction) 3. HADS 4. EQ-5D 5. Death 6. Hospitalisation 7. Institutionalisation 8. Costs based on Client Service Receipt Inventory
Starting date	18/02/2008

Contact information	Dr Anne Forster Academic Unit of Elderly Care and Rehabilitation Temple Bank House Bradford BD9 6RJ Tel: +44 (0)1274 383 406/401 Fax: +44 (0)1274 382 766 Email: a.forster@leeds.ac.uk

Forster 2008⁴²⁵

Study name	Stroke system of care trial: a cluster randomised trial evaluation of a patient and carer-centred system of Longer-Term Stroke Care (LoTS Care)
Methods	A pragmatic, multi-centre cluster randomised controlled trial
Participants	<p>Inclusion criteria</p> <p>A stroke service will only be considered for inclusion in the trial if it includes a stroke unit which fulfils the Royal College of Physicians guidelines definition of a stroke unit, that is, by the presence of 4/5 of the following criteria:</p> <ol style="list-style-type: none"> 1. Consultant physician with responsibility for stroke 2. Formal links with patient and carer organisations 3. Multidisciplinary meetings at least weekly to plan patient care 4. Provision of information to patients about stroke 5. Continuing education programmes for staff <p>Stroke Care Co-ordinators:</p> <ol style="list-style-type: none"> 1. A registered healthcare professional with documented experience in stroke care 2. Undertakes a community based liaison or co-ordinating role for stroke patients 3. Co-ordinates a range of longer-term care inputs on the patients' and carers' behalf (e.g. signposting, carrying out assessments) 4. Works within a stroke service as above <p>Patients:</p> <ol style="list-style-type: none"> 1. Confirmed primary diagnosis of stroke 2. Referred to a SCC on discharge home from hospital or within six weeks of stroke 3. Waiting for their first SCC assessment visit 4. Provide written informed consent or carer assent <p>Carers</p> <ol style="list-style-type: none"> 1. Identified by the patient 2. Eligible for this study <p>Exclusion criteria</p> <p>Patients:</p> <ol style="list-style-type: none"> 1. Unlikely to survive for more than three months 2. Discharge to/resident in a nursing or residential home 3. Previously registered to the trial

	4. Taking part in other stroke research network adopted studies which involve 6- and 12-month follow-up questionnaires
Interventions	<p>SCCs in stroke services randomised to the intervention group will be trained to deliver a system of care centred on key problems identified as of central importance to stroke patients and their carers. The assessment schedule is presented in a manual comprising 16 questions (patient) and 11 questions (carer) representing the identified problem areas, linked to reference guides containing educational text with algorithms of evidence based treatment options and associated patient carer action plans. Implementation of the assessment system is supported by a specific training programme.</p> <p>SCCs in stroke services randomised to the control group will continue to deliver current community-based practice as determined by local policy and practice.</p>
Outcomes	<p>Primary outcome General Health Questionnaire 12 (GHQ12) completed by the patient six months after recruitment.</p> <p>Secondary outcome measure(s) Patients at 6 and 12 months:</p> <ol style="list-style-type: none"> 1. Frenchay Activities Index 2. Barthel Index 3. EQ-5D 4. Stroke Impact Scale 5. Longer-term Unmet Need in Stroke 6. Satisfaction 7. Death 8. Hospital re-admission 9. Institutionalisation 10. Total costs 11. Cost-effectiveness/cost-utility <p>The GHQ12 at 12 months is also a patient secondary outcome measure to assess whether any intervention effect is sustained.</p> <p>Carers at 6 and 12 months are:</p> <ol style="list-style-type: none"> 1. GHQ12 2. Carer Burden Scale 3. Satisfaction 4. Death 5. Institutionalisation
Starting date	01/06/2008
Contact information	<p>Dr Anne Forster Academic Unit of Elderly Care and Rehabilitation Temple Bank House Bradford BD9 6RJ Tel: +44 (0)1274 383 406/401</p>

	Fax: +44 (0)1274 382 766 Email: a.forster@leeds.ac.uk

Graven 2008⁴²⁶

Study name	From rehabilitation to recovery: A model to optimise consumer and carer involvement in the first year post stroke.
Methods	Randomised controlled trial
Participants	Inclusion criteria Patient admitted for rehabilitation with a primary diagnosis of acute stroke. Carers. Minimum age = 18 Exclusion criteria Discharge from rehabilitation to nursing home. Primary cause of disabilities is a diagnosis other than stroke. Living more than one hour travel time from St.Vincent's Health Melbourne.
Interventions	Experimental intervention Collaborative goal setting with the patient and carer prior to discharge from rehabilitation. Monitoring of goal achievement and barriers to goal achievement. Collaborative problem solving to overcome barriers. Facilitated referral to health and community agencies, tailored to needs. Promotion of healthy and active lifestyles. Promotion of self efficacy and self reliance. Providing targeted carer support through information provision, emotional support and practical support tailored to needs over a 12 month period. Minimum of four interventions, maximum twelve. Comparator intervention Usual care plus phone contact with an allied health practitioner on three occasions for general support and encouragement.
Outcomes	Primary outcome Carers: Quality of Life, 6 and 12 months Stroke survivors: Geriatric Depression Scale, 6 and 12 months Secondary outcomes, 6 & 12 months Carers: Family Burden Interview Stroke survivors: Functional Independence Measure (motor subset), Minimental State Examination, London Handicap Scale, Activity card sort, Strategies used by people to promote health scale.
Starting date	1/03/2008
Contact information	Christine Graven Physiotherapy Department St.Vincent's Health Melbourne PO Box 2900

	Fitzroy 3065 Victoria Australia Tel: (03) 9288 3827 Email: Christine.GRAVEN@svhm.org.au

Hautzinger 2007⁴²⁷

Study name	Telephone-based behaviour-therapeutic intervention to reduce family carer burden in chronic stroke (Telefongestützte verhaltenstherapeutische Intervention zur entlastung Pflegenden angehöriger von Schlaganfall-betroffenen)
Methods	Prospective randomised controlled trial
Participants	<p>Inclusion criteria</p> <p>Care recipient:</p> <ol style="list-style-type: none"> 1. 60 years or older at the time moment of index stroke* (loss of neurological function due to an Ischaemic or haemorrhagic intracranial vascular event) 2. Formal need of care or help for at least 1.5 hours a day (10.5 hours per week) (this time criteria corresponds to the criteria for receiving benefits from the statutory German nursing insurance), or 3. Need of care in form of supervision or for care recipients with cognitive impairment for at least 1.5 hours a day (10.5 hours per week) (these people are currently not adequately considered by the statutory German nursing insurance, but might be in the future) <p>Carer:</p> <ol style="list-style-type: none"> 1. Age: 18 years and older 2. Family member, who has cared for the stroke survivor for at least six months 3. Time spent with care of stroke survivor (including nursing care, supervision and contact) at least 1.5 hours per day or 10.5 hours per week. There can be additional support with care (e.g. professional community nurses) 4. Significant carer burden assessed with six screening questions 5. Living in the region of Stuttgart (maximum of one hour with public transport from the study centre) 6. Availability of a telephone extension 7. At enrolment, plan to remain in area for the duration of the intervention 8. Ability to communicate over the telephone <p>* In the case of recurring strokes the index stroke is defined as the last stroke that increases the demand of care in a significant way</p> <p>Exclusion criteria</p> <p>Care recipient:</p> <ol style="list-style-type: none"> 1. Planned nursing home placement within the next six

	<p>months</p> <ol style="list-style-type: none"> 2. Unstable or progressive severe disease 3. Terminal status based on a prognosis of less than six months <p>Carer:</p> <ol style="list-style-type: none"> 1. Duration of care giving for the stroke survivor more than five years after index stroke 2. Mental disease like schizophrenia, alcohol addiction or cognitive impairment (rapid dementia screening test less than nine points) 3. Severe and unstable or progressive diseases like cancer 4. Not able to understand and speak German language 5. Temporary increased carer burden because of an acute illness (greater than repetition of the screening after such an episode of increased burden) 6. Involved in another clinical trial of interventions for carers (non-drug study)
Interventions	<p>Intervention group:</p> <p>Telephone-based problem solving training over 12 months. It comprises two home visits (after randomisation and month three) and regular telephone contacts with decreasing frequency over 12 months:</p> <ol style="list-style-type: none"> 1. Month one: weekly 2. Months two to three: biweekly 3. Months 4 to 12: monthly, plus up to four additional optional contacts <p>The problem solving procedure is structured into the following six steps using different cognitive-behavioural techniques like cognitive restructuring and communication skill training according to a fixed intervention manual:</p> <ol style="list-style-type: none"> 1. Problem definition and facts 2. Optimism and orientation 3. Goal setting 4. Generation of alternatives 5. Decision making 6. Implementation and verification <p>For initial problem orientation a card sorting procedure with 40 cards is used. The intervention is delivered by a psychologist.</p> <p>Intervention and comparator group:</p> <p>All participants receive a monthly information letter by post on care-giving or stroke related issues (i.e., carer rights, nutrition, relaxation techniques) over one year.</p> <p>Interventions and assessments are delivered by different teams; the assessment team is blinded to the different groups by the study centre. Because communicating of their status by the participants a complete blinding is</p>

	probably not possible.
Outcomes	<p>Primary outcomes</p> <ol style="list-style-type: none"> 1. Subjective carer burden (Sense of Competence Questionnaire [SCQ]) 2. Carer depression (the Centre for Epidemiological Studies Depression scale [CES-D]) 3. Total costs of formal and informal care 4. Indirect costs <p>Measured at: T0 (Agreement) primary and secondary outcomes T1 (3 ½ months after T0) primary and secondary outcomes T2 (12 months after T0) primary and secondary outcomes T3 (24 months after T0) and T4 (36 months after T0) institutionalisation rates</p> <p>Secondary outcomes</p> <ol style="list-style-type: none"> 1. Ability of social problem solving 2. Social activities 3. Social support 4. Subjective physical symptoms 5. Burden of behavioural symptoms 6. Subjective health related quality of life 7. Qualitative analysis of carer burden with description of main problem areas with the card set 8. Institutionalisation rates of care recipients over a prolonged observational period <p>Measured at: T0 (Agreement) primary and secondary outcomes T1 (3 ½ months after T0) primary and secondary outcomes T2 (12 months after T0) primary and secondary outcomes T3 (24 months after T0) and T4 (36 months after T0) institutionalisation rates</p>
Starting date	01/03/2007
Contact information	<p>Professor Martin Hautzinger Abteilung für Klinische Psychologie und Entwicklungspsychologie Universität Tübingen Christophstr. 2, Tübingen, Germany hautzinger@uni-tuebingen.de</p>
Notes	
MAPSS 2006 ⁴²⁸	
Study name	Improving stroke recovery in Maori and Pacific people and their families (MAPSS)
Methods	Multicentre randomised controlled trial
Participants	<p>Inclusion criteria Stroke using World Health Organisation definition 'rapidly developing symptoms and/or signs of focal, and at times global, loss of cerebral function, with symptoms lasting longer than 24 hours or leading to death with no apparent</p>

	<p>cause other than that of vascular origin. Self identified ethnicity as Maori, Samoan, Tongan, Cook Island Maori, Niuean or Fijian. Aged ≥ 18.</p> <p>Exclusion</p> <p>Cannot give informed consent. Living within institution after stroke. Subarachnoid haemorrhage.</p>
Interventions	<p>Randomised controlled trial (multi centre). Participants randomised to receive one of three interventions or a control. Intervention A - Educational video lasting 80 minutes Intervention B - goal setting exercise lasting 90 minutes Intervention C - both the video and the goal setting exercise lasting 170 minutes</p> <p>Comparator intervention: written pamphlet will take 30 minutes to read</p>
Outcomes	<p>Primary outcome at 6 and 12 months</p> <p>Short form 36 (SF-36)</p> <p>Secondary outcomes at 6 and 12 months</p> <p>Carer strain index</p> <p>Mortality</p> <p>Mental wellness (using Hua Oranga)</p> <p>Frenchay Activity Index</p> <p>Barthel Index</p> <p>Charlson Comorbidities Index</p> <p>Discrimination (EDQ)</p>
Starting date	1/02/2006
Contact information	<p>Dr Matire Harwood</p> <p>c/o Medical Research Institute of New Zealand (MRINZ) PO Box 10055 Wellington, New Zealand</p> <p>Tel: +64 4 4729112</p> <p>Email: matire.harwood@mrinz.ac.nz</p>

Markle-Reid 2007⁴²⁹

Study name	The Comparative Acceptability, Safety, Effects and Expense of Specialized, Integrated, and Interdisciplinary Community Rehabilitation for Stroke Survivors and Their Carers
Methods	<p>Type: Interventional</p> <p>Study Design: Allocation: Randomised</p> <p>Control: Active Control</p> <p>Endpoint Classification: Efficacy Study</p> <p>Intervention Model: Parallel Assignment</p> <p>Masking: Double Blind (Investigator, Outcomes Assessor)</p> <p>Primary Purpose: Treatment</p>
Participants	<p>Inclusion Criteria: diagnosis of stroke has been confirmed through admission to an acute care hospital (defined as an acute focal neurological deficit caused by cerebrovascular disease).</p> <ul style="list-style-type: none"> newly referred to an eligible for home care services (physiotherapy, speech language therapy, occupational therapy, and nursing) through the Toronto CCAC, from acute care or in-patient stroke

	<p>rehabilitation hospitals.</p> <ul style="list-style-type: none"> • living at home in the community (outside of an institutional setting) up to 18-months post-stroke. <p>Exclusion Criteria:</p> <ul style="list-style-type: none"> • refuse to give informed consent. • more than 18 months post-stroke at time of recruitment. • unable to read/write English and an appropriate translator is not available. • must be English speaking
Interventions	<p>Experimental: Participants in the experimental group will receive home care services from a team of professional service providers (CCAC Care Coordinator, Registered Nurse, Occupational therapist, Physiotherapist, Speech language pathologist, Nutritionist) and non-professional service providers (personal support workers) with experience and training in stroke care. The team will provide a comprehensive, coordinated and evidence-based approach to stroke rehabilitation through weekly case conferencing, a written interdisciplinary care plan, and joint visits.</p> <p>Control: No intervention</p>
Outcomes	<p>Primary Outcome Measures: SF-36 Health Survey Secondary Outcome Measures: Stroke Impact Scale - 16 Reintegration to Normal Living Index Short Portable Mental Status Questionnaire Centre for Epidemiological Studies in Depression Scale Carer Reaction Assessment Scale Personal Resource Questionnaire Health and Social Services Utilization Inventory Kessler</p>
Starting date	February 2006
Contact information	Maureen Markle-Reid email: mreid@mcmaster.ca
Notes	Recruitment stopped but study ongoing. 7th April 2010/

Teel 2005^{430;431}

Study name	Promoting Stroke Carer Health Vis Self Care TALK: Education and Support Telephone Partnerships With Nurses
Methods	A randomised, treatment/comparison, repeated-measures experimental design.
Participants	Older (55 years or older), spousal carers of persons with stroke. Participants must be living with and caring for the stroke survivor, and the stroke must have been a first-ever stroke, occurring 6-36 months prior to enrolment.
Interventions	Self-Care TALK is a behavioural intervention. Self-Care TALK involves 6 weekly semi structure telephone sessions with an advanced practice nurse. Written materials are available for use during the Self-Care TALK sessions. Sessions focus: healthy habits, building self-esteem, focusing on the positive, avoiding role overload,

	communicating, and building meaning.
Outcomes	Primary Outcome Measures: SF-36v2, PCS (perceived physical health) SF-36v2, MCS (perceived mental health) [Time Frame: 2 months and 6 months post enrolment] Secondary Outcome Measures: M-CSI: modified (carer strain), SRAHP (self efficacy for health), CED-D (depression) [Time Frame: 2 and 6 months post enrolment]
Starting date	July 2005
Contact information	Cynthia Teel PhD RN, University of Kansas School of Nursing,
Notes	None

Table 5-4 Characteristic of studies waiting assessment

FITT 1998^{432;433}

Methods	Randomised controlled trial
Participants	Inclusion Criteria Patients hospitalized with an MRI or CT confirmed stroke or definitive hemiplegia will be eligible for this trial. Exclusion Criteria Patients with subarachnoid hemorrhage (SAH), transient ischemic attack (TIA), or subdural hematoma, who have a comorbidity severe enough to warrant hospitalization within the 3 months prior to stroke, who have a functional psychosis, who do not have a carer, who were admitted to the hospital from nursing home, and who cannot speak English, will be ineligible for this trial.
Interventions	All patients will receive standard medical care in the hospital. Eligible patients will be randomised to receive either FTIT or no intervention after discharge. The patients in the FTIT group will be contacted by telephone every week for 6 weeks, every 2 weeks for 2 months, and then monthly for 2 months. During these calls, the study clinician will inquire as to how the participants are doing, and will address any questions and concerns. All patients will be re-evaluated 6 months after discharge.
Outcomes	Changes in thinking, concentration, attention, memory, mood, and family functioning.
Notes	Trial started in 1998. Unable to track the Principal Investigator Ivan W. Miller, PhD, Rhode Island Hospital Providence, Rhode Island 02769 Contact Email Ivan_Miller@brown.edu

Main 1990^{434;435}

Methods	Randomised controlled trial
Participants	Stroke survivors and carers
Interventions	To test whether information giving or counselling help

	stroke survivors and their carers. Suitable subjects are randomly allocated to three groups. The control group receive routine care. The information group receive all routine care plus the information pack and an opportunity to discuss the contents of the pack. The counselling group receive the information pack and 8 sessions of counselling.
Outcomes	Emotional and social adjustment in carers and stroke survivors, change in mental state and physical dependency
Notes	Contacted Alistair Main (co-author). No additional information available. Abstract published in 1993.

Ostwald 2007⁴³⁶

Methods	Randomised controlled trial
Participants	<p>Inclusion Criteria: Patient experienced a stroke within the last year, age 50 or older, going home with a spouse or committed partner, needs daily assistance, live within 50 miles of the Texas Medical Centre, can be reached by telephone, able to understand English</p> <p>Exclusion Criteria: Admitted from or being discharged to a nursing home, disability requiring total assistance, lethargic, obtunded or comatose other significant CNS disease (i.e., severe Parkinson's), severe psychopathology, globally aphasic, other major illness that would interfere with rehabilitation (i.e., advanced cancer).</p>
Interventions	This 5-year randomised intervention study uses an advanced practice nurse, with the assistance of an interdisciplinary rehabilitation team, to provide education, support, skill training, counselling, and social and community linkages to stroke survivors and their spouses for 6 months post-hospital discharge. The intervention will be delivered using previously tested protocol guidelines. No information available on comparator.
Outcomes	<p>Primary Outcome Measures: Stroke survivor function Stroke survivor and carer quality of life Stroke survivor and carer stress Stroke survivor and carer depression Service utilization Cytokine levels of carers</p> <p>Secondary Outcome Measures: Family coping styles Social support system Carer preparation Marital relationship</p>
Notes	Contacted Principal investigator Sharon K. Ostwald for further information. No response.

Chapter 6 Conclusions

‘Informal (and unpaid) care plays a vital role in the support of older people. Very large numbers of people provide at least some level of care, with some providing a very substantial input. Key questions are: Should we continue to rely on informal care? If so what are the consequences? Are the resultant situation and outcomes for carers reasonable?’

THE KING’S FUND, Securing good care for older people, 2006

6.1 Summary of the findings

6.1.1 Chapter 2 *Is informal care giving independently associated with poor health? A population-based study.*

The analysis of the UK Census 2001 data set found that 8.3% of non-caregivers report poor health compared to 9.0% of those who provide care (OR 1.100, 95% CI 1.096-1.103). An odds ratio of 1.1 indicates that the odds of self-reported poor health in those people who are exposed to providing informal care are 10% higher than those who not exposed to providing informal care. This association remained after adjusting the analysis for gender, age, marital status, ethnic group, economic activity and educational attainment. Moreover, this study showed a monotonic trend in self-reported poor health frequency with increasing levels of self-reported exposure to providing informal care. However, associations that show a dose response relationship are not necessarily causal. Confounding can produce a dose-response relationship between the self-reported exposure to informal care and self-reported poor health outcome if the confounding factor itself exhibits a dose-response relationship with self-reported poor health. Moreover, the UK Census 2001 is in effect a cross sectional study which includes everyone in the UK population at the time of ascertainment; therefore exposure to providing informal care is ascertained at the same time as self-reported poor health.

As far as is known, this is the first time the UK Census 2001 data has been used to develop logistic models with the aim of quantifying the effects of informal care as a predictor of self-reported poor health. However, these results are

consistent with suggestions that exposure to informal care may be a predictor of poor health.

6.1.2 Chapter 3 The Glasgow Carers Cohort Study: informal care giving and risk of disease

The Glasgow Carers Cohort Study (GCCS) consisted of 26 exposed subjects (carers) and 43 age sex matched unexposed subjects. Mean age at entry was 54.1 for the exposed group and 59.1 in the unexposed group. Stress was more prevalent in the potentially exposed cohort at recruitment. There were no significant differences in deprivation, economic activity, educational attainment, and prescription drug, alcohol and tobacco consumption. An increased risk ratio (RR) related to exposure to providing informal care was seen for the primary outcome of perceived stress (RR 7.02; 95% confidence interval (CI) 1.65 to 29.85). Therefore, risk of stress was 7.02 times greater in the group exposed to providing care compared to the non exposed group. Exposed subjects were significantly less happy than unexposed participants at three and six months. No significant differences in the level of depression or severity of somatic symptoms between exposed and unexposed groups were found at three and six months. Therefore, providing care to stroke survivors during the six month period post hospital discharge is associated with a substantial increase in perceived stress. However, this may be confounded by the sense of shock and disorientation caused by a stroke in the family, or a close social network. Further, people who provide care to stroke survivors living in the community a minimum of three months post hospital discharge are significantly less happy than their non-care giving counterparts.

The majority of people who were recruited to the GCCS were exposed to providing care at one or both three and six month observation time points. The informal care exposure appears to be a chronic in that the exposure persists over a prolonged period of time⁴³⁷. There is evidence from this research that individuals may experience various levels of informal care exposure, which may change over time and follow no particular pattern.

6.1.2.1 Comparison of findings from other studies

As far as is known, this is the first study of the perceived stress effects of providing care to stroke survivors. The results from this study are similar to those of Esterling et al.,⁴⁵¹ which investigated the long-term physiological effects of chronic stress in 14 continuing or current carers of individuals with Alzheimers disease, 17 former carers of individuals with Alzheimers disease and 31 non-caregiving individuals. This study found higher levels of perceived stress as measured by the PSS-14, in the continuing carer group (MD 8.49 (95%CI, 6.23, 10.75, $p < 0.001$) compared to the non-care giving group and higher levels of perceived stress in the bereaved carer group (MD 5.71 (95%CI, 2.07, 9.35, $p = 0.002$)) compared to the non-care giving group. However, unlike the participants in the GGCS which had a maximum of six months experience of providing informal care, the participants in the Esterling study had a minimum of five years experience of providing informal care to a family member with Alzheimers disease. This raises the question as to whether the stress effects of providing informal care to stroke survivors extend beyond the six month follow-up period of the GGCS. Furthermore, in contrast with the findings from the GGCS study, this study found higher levels of depression in the continuing carer group and bereaved carer group compared to the non-care giving group. This suggests that for people who provide informal care to stroke survivors, the period of time between causal action until depression onset (the induction period) may be longer than six months, if at all.

One of the weaknesses of the Esterling study was lack of a clear definition of what is a current informal carer.

6.1.3 Chapter 4 Incidence, prevalence and association between providing informal care-giving to stroke survivors and depression: a systematic review and meta-analysis

1624 titles and abstracts were screened. 120 were identified for further detailed examination. 18 studies met the inclusion criteria. One study is still awaiting assessment. No studies that met the inclusion criteria either included a healthy control group with no history of depression (case-control studies) or

included a referent group of people who were unexposed to providing informal care (cohort studies) or studies that included populations not selected on the basis of either exposure to care-giving or depression. No investigators reported including participants to cohort studies that were free of depression at the initial observation. 12 studies used a prospective cohort design and six studies used a cross sectional design. Mean age of participants ranged from 41.2 years to 66.9 years and between 62% and 91% of participants were women. All studies used valid and reliable self-report rating scales for depression. No studies reported a precise specification of informal care. No study reported measuring informal caregiver status at first follow-up assessment. 16 of the 18 studies generated prevalence data. Data was not available for two studies. The estimates of prevalence of depression are based on the number of people who scored above a clinical cut point on a self-report dimensional rating scale for depression. The overall pooled prevalence estimate calculated using the inverse variance method using a random effects model was 28% (95% CI 23%, 33%) with significant statistical heterogeneity ($p < 0.001$) and 81% of the observed variability was due to between-study differences and not variability due to sampling error ($I^2 = 81\%$).

In summary, this systematic review of incidence, prevalence and risk of depression in people who provide care to stroke survivors revealed that while depression may be common in people who provide care, there is insufficient evidence to determine if exposure to providing care is a cause of depression. Lack of a detailed definition for an informal carer is common to all studies and affects interpretability of results.

6.1.3.1 Comparison with findings from other studies

A narrative review and analysis by Han and Haley¹³⁶ found seven studies providing estimates of the prevalence of depression among stroke caregivers. They report that the prevalence of depression in informal caregivers ranges from 34% to 52%. This review found more studies providing estimates of depression and a pooled estimate of prevalence which was lower than the range reported by Han and Haley. The difference may be due to, the extensive searching and explicit and strict inclusion criteria used in this review. One systematic review of depressive disorders in carers of people with dementia⁴⁴⁴ excluded primary

studies which used self-rated scales of depressive disorder symptomatology and therefore is not comparable with the findings from this review. In both reviews lack of a clear definition of a current informal carer was an issue.

6.1.4 Chapter 5 Non-pharmacological interventions for informal carers of stroke survivors

22713 titles and abstracts were screened. Eight studies including a total of 1007 participants met the inclusion criteria. In view of the diverse nature of interventions, individual studies were independently assigned to one category of intervention: teaching procedural knowledge/ 'vocational training', support and information, psycho educational. The results of all the studies were not pooled because of substantial methodological, statistical and clinical heterogeneity. For the primary outcome of caregiver's stress or strain, no significant results within categories of intervention were found, with the exception of one single centre study examining the effects of a 'vocational training' type intervention which found a mean difference between the intervention and comparator group at the end of scheduled follow-up of -8.67 (95% confidence interval -11.30 to -6.04, $p < 0.001$) in favour of the 'teaching procedural knowledge' type intervention group. As there was substantial methodological, statistical and clinical heterogeneity across all the secondary outcomes (global measures of stress or distress, anxiety, depression, satisfaction, mortality) it was decided that it was inappropriate to combine the results of studies. No significant results within categories of interventions with the exception of one single centre study assessing the effects of a vocational training intervention which demonstrated that participants who received 'the vocational training' type intervention had fewer symptoms and signs of depressive disorder, less anxiety and a better health related quality of life than those who did not receive the intervention. One limitation across all studies was the lack of a description of important characteristics that define the informal caregiver population.

This systematic review of non-pharmacological interventions for people who provide care to stroke survivors revealed that the only intervention with any promising evidence at present is a 'vocational training' type intervention. However, this is based on the results from one small, single centre study.

6.1.4.1 Comparison with findings from other studies

One narrative review³³¹ and one systematic review and meta-analysis³³⁶ found insufficient evidence from high quality studies to draw conclusions. In contrast, this review found ‘vocational training’ type interventions were the most promising interventions.

6.2 Rationale for the approach taken to this overall study

‘Now that you have a pretty good idea of the question you want to ask, it's time to use the Scientific Method to design an experiment which will be able to answer that question. If your experiment isn't designed well, you may not get the correct answer, or may not even get any definitive answer at all.’

The Scientific Method: A helpful guide by Science Made Simple, 2011

The overall goal of this thesis was to obtain valid and precise estimates of the frequency of adverse health outcomes and the effect of the exposure (i.e., informal care as a behaviour or an intervention such as ‘education’) on the occurrence of adverse health outcomes in informal carers.

I have a strong background in evidence-based health care (EBHC). One of the fundamental skills gained practising EBHC is the ability to ask of clearly focused and well-built research questions. The benefits of having this ability are it is easier to search for the evidence and to choose the most appropriate study design to answer the question. The research question provides the foundation upon which the study design, the study conduct and data analysis is built.

This overall study includes four distinct component parts, each addressing different research questions and each using what has been determined as the most appropriate research methods to answer each question. However, the basic questions are simple; having to provide what is necessary for the health, welfare, maintenance and protection of another in ill health, frailty or disability is frequently viewed as hazardous to the informal carers health...what scientific evidence is available to support this assertion? And, if there is evidence from epidemiological studies of high quality that the informal care exposure is

hazardous to the informal carers health, what is the magnitude of the risk and what steps can be taken to preserve the health of the informal carer?

Cost restrictions and limitations imposed by ethics restricted the research included in this study to non-experimental study designs (cohort study) and use of secondary data (UK Census 2001 data set). Systematic review and meta-analytic methods provided a rigorous and coherent approach for merging and contrasting results from previous primary studies addressing the same or similar questions. Informal carers of stroke survivors were chosen as the main source population for study as stroke is the most common cause of complex disability. An extensive review of the biomedical informal care literature and social sciences informal care literature pointed in two different directions of study; the biomedical literature pointed in the direction of stress as an important effect of providing informal care and the social science literature pointed in the direction of depression as an important effect of providing informal care. The multiple study designs used in the thesis required in depth knowledge of study design and conduct, issues of validity (confounding, selection and information bias) and issues of precision in epidemiological studies and data analysis. While there are concepts and methods which are central to the discipline of epidemiology, the breadth and depth of knowledge required to perform all studies to a high level was challenging. Moreover, the broad scope of illness studied required specific and detailed knowledge about the aetiology; epidemiology and rating scales used for the measurement of the occurrence of each illness studied which was demanding.

6.3 Lessons learned

6.3.1 Chapter 2 Is informal care giving independently associated with poor health? A population based study

6.3.1.1 Lessons learned: Limitations of using secondary data from the UK Census 2001 for aetiological inference

The UK Census 2001 data is collected population and other statistics for the purpose of planning and the allocation of resources. Users of UK Census data

include national and local government and health and education providers. Therefore, the UK Census 2001 data was generated for purposes different from the objective of this study. Nonetheless, it is possible to use the UK Census 2001 data to shed light on the relationship between self-reported informal care and self-reported poor health. However, there are a number of limitations.

When it comes to aetiological inferences it is crucial to take account of the weaknesses of the cross sectional nature of the UK Census 2001 design. First, it is likely that cases of self-reported poor health with long duration were over represented and cases of self-reported poor health with short duration were under represented. For example, if exposure to providing informal care is self-reported poor health which could be described as mild and long-lasting (as opposed to severe and rapidly fatal) so that exposure to informal care is positively associated with duration of self-reported poor health and the prevalence of self-reported exposure to informal care will be higher amongst those reporting poor health. Moreover, the UK Census 2001 does not collect data on other potentially important determinants of self-reported poor health such as health behaviours (diet, exercise, alcohol consumption, and smoking), the presence of co morbidity or body mass index which are unmeasured confounders, therefore, confounding (or mixing of effects) is likely to be a problem. However, even in the event that these data were collected during the UK Census, issues of disclosure made it highly unlikely that all potentially important variables would be made available for inclusion in a multivariate analysis. Moreover, because the UK Census 2001 is a cross sectional design, it is impossible to determine the time order of events, does exposure to providing informal care precede self-reported poor health or vice versa?

6.3.1.2 Lessons learned: the strengths of using UK Census 2001 data

The UK Census 2001 data is a good source of study data. The data set is large and therefore random error is reduced. Response rates are high and therefore selection bias is reduced. The data is relatively cheap to acquire, its moderately easy to access, although a license is required, the user specifies the data required, the data are presented in a format (grouped data) which allows it to be easily uploaded and analysed into some (Minitab, SAS) but not all statistical packages (SPSS) and it avoids the need for data collection which is

likely to be expensive, time consuming and involve potentially low response rates.

6.3.1.3 Conclusions

Use of the data from the UK Census 2001 illustrates how a large and valid secondary data source can be activated within a short period of time to quantify the effect of self-reported informal care on self-reported poor health and to generate further research questions. However, confounding by unmeasured factors was a considerable problem when attempting to quantify the effects of self-reported informal care as a predictor of self-reported poor health using the UK Census 2001 dataset. This needs to be taken into account when considering using the UK Census 2011 data set for the same purpose. However, the UK Census data set is a fabulous data set to learn about the principles and practice of statistics for research, with particular reference to logistic regression.

6.3.1.4 Lessons learned: if I could start again

If I could start again I would:

- Still use the UK Census 2001 data set as a resource for learning about the concepts and techniques of logistic regression.
- Think twice about using the data set for aetiological inference.

6.3.2 Chapter 3 The Glasgow Carers Cohort Study: informal care giving and risk of disease

6.3.2.1 Lessons learned: limitations of the GCCS

The study was underpowered. While the expected mean difference between the exposed 'informal care' group and the 'unexposed' non care-giving group on the primary outcome of Perceived Stress was anticipated to be much smaller than the actual effect (anticipated mean difference = 2.5 assuming a common standard deviation of 6.5, actual difference = 6.5). Small numbers limited the ability to explore the influence of other important covariates on the primary

outcome of perceived stress. While every attempt was made to ensure that target recruitment numbers were achieved, it is possible that this study was over ambitious given the time scale and resources available.

In addition, the use of a simple ordered categorical measure of informal care exposure (0 hours per week, 1-19 hours per week, 20-49 hours per week and 50+ hours per week) limited the flexibility in data analysis and may not have adequately measured the amount of informal care exposure as it relates to the development of ill health. This type of random error measurement in the exposure can lead to attenuation or flattening of the slope of the line describing the relationship between the informal care exposure and the ill health outcome. Future studies should collect numerical data on informal exposure.

6.3.2.2 Lessons learned: strengths of the study

The strengths of the study include the use of matching. The purpose of matching was to ensure that the exposed and unexposed participants had very similar age and sex characteristic to prevent an association between age and the 'care-giving' exposure and sex and the 'care-giving' exposure at the start of follow-up and therefore prevent confounding of the crude risk difference and risk ratio. However, matching did not remove the need to control for the matching factors in the analysis. In addition, the benefits of matching (including improved statistical efficiency, i.e., a decrease in the standard deviations of the effect estimates) were not guaranteed as the exposure was not randomly allocated.

Other strengths include limited loss to follow-up in both exposed and unexposed groups which may be in part due to the multiple strategies used for gaining cooperation and maintaining a high response rate for example: phone calls highlighting the imminent arrival of the next questionnaire, use of distinctive colours in all correspondence and hand applied postage stamps on all correspondence.

6.3.2.3 Lessons learned: practical issues

This matched cohort study required a large number of participants which in practice was difficult to recruit given the timescale and available resources. Matching was also an expensive and time consuming process.

Participant identification and recruitment was challenging because of the need to involve certain organisations (SPCRN, SPCRN, Townhead Health Centre General Practice) in the process. Each individual organisation has its own mission and objectives i.e., each organisation is structured in a different way, each organisation has different policies and objectives that they seek to fulfil, each organisation is managed differently and each organisation seeks to serve different stakeholder interests. Difficulties always arise when there is inherent competition between groups (recruitment to drug trials vs. recruitment to trials of rehabilitation interventions vs. recruitment to epidemiologic studies of informal carers) for crucial but scarce resources.

6.3.2.4 Conclusions

Although expensive and time-consuming, the matched cohort study design did offer many benefits particularly given that the randomised controlled trial was not possible because of the nature of the exposure.

6.3.2.5 Lessons learned: if I could start again

If I could start again I would:

- Increase the recruitment rate by actively increasing the number of people approached to take part at each individual recruitment site and take on more recruitment sites. However, the recruitment agencies (Scottish Stroke Research Network and the Scottish Primary Care Research Network) would remain the same and therefore it is likely that the same issues of competition between different types of studies for attention would persist.

- Like to have access to a ‘bank’ of people who have already consented to act as controls or members of a referent group.
- Develop an informal care exposure measurement system which would include a clear definition of the index condition of a current informal caregiver which may include the frequency of informal care activity (number of activities per day), the duration of informal care activity (weeks or months), the intensity of activity (types of activity performed) and age at the providing informal care began. I would also define the absence of the informal care exposure or the ‘reference condition’ - with regard to frequency, duration, intensity and induction period.
- Classify each participants informal care exposure experience in different exposure categories at different times.
- Like to use stratified analysis methods to analyse the cohort data. This would require that the recruitment strategy yield uniquely matched exposed and unexposed participants.
- Like to learn how to calculate adjusted risk ratios for summarising the results of the cohort study. Risk ratios are much more intuitive and clinically meaningful than odds ratios.

6.3.3 Chapter 4 Incidence, prevalence and factors associated with depression in people who provide care to stroke survivors and the effect of exposure to providing care to stroke survivors on the occurrence of depression: a systematic review and meta-analysis.

6.3.3.1 Lessons learned: benefits and drawbacks of systematic reviews of epidemiological studies

A decision was made early on in the design of the protocol for this review to exclude studies with a randomised controlled design as these studies are usually

designed to answer questions on the effects of interventions targeted towards highly selected patient groups or populations.

The benefits of systematic review work include a fully worked up protocol prior to starting the review proper, meaning that all concepts, methodological issues and statistical techniques for merging and contrasting results across studies are worked out and defined in advance. However, while the approach is the same, unlike systematic reviews of interventions there is no equivalent of the Cochrane review groups for systematic reviews of epidemiological studies. Therefore, there is no support in terms of searching the literature for relevant studies, there are no standards to adhere to, there is no methodological support and there is over arching body checking to see if the review is carried out appropriately. In addition, there is also no stringent peer review process to ensure the quality and appropriateness of the review. In addition, unlike systematic reviews and meta-analysis of interventions, meta-analysis of the epidemiologic literature is not as well developed as for randomised controlled trials. Therefore systematic review and meta-analytic concepts and techniques had to be developed, adapted or refined in order to carry out this review and meta-analysis.

6.3.3.2 Lessons learned: if I could start again

If I could start again I would:

- Be very grateful for the systematic review and meta-analysis template for epidemiological studies that has been developed for this study. The template that has been developed for this review is easily transferrable to systematic reviews and meta-analysis addressing the same or similar questions.

6.3.4 Chapter 5 Systematic review and meta-analysis of the effects of non-pharmacological interventions delivered to informal caregivers of stroke survivors

6.3.4.1 Lessons learned: benefits and drawbacks of systematic reviews of interventions

In direct contrast to the systematic review and meta-analysis of depression and informal carers (Chapter 4), this systematic review was carried out under the auspices of The Cochrane Stroke Group (CSG) with all the attendant support and resources. This made the review much more straightforward to carry out.

6.3.4.2 Lessons learned: the focus of interventions, beyond the informal carer

Randomised controlled trials of Interventions which may impact on informal carers of stroke survivors come in four categories: 1) interventions delivered to informal carers of stroke survivors 2) interventions delivered to informal carers and stroke survivors 3) interventions targeted towards stroke survivors with the intention of having an impact on informal carers and 4) interventions delivered to health or social care professionals with the intention of having an impact on informal carers or stroke survivors.

This systematic review focused on the first two categories, where the emphasis is on changing some aspect of the informal carer. However, results from a recent (as yet unpublished) qualitative study suggests one source of stress is the health and social care professional environment in which the informal carer engages or operates. Another source of stress or difficulties for informal carers is dealing with bureaucratic organisations (such as banks) and bureaucratic decisions (such as stroke survivor assessed to no longer meet the requirements of a government scheme for special car parking badges). In summary, if preserving the health of the informal carer is a serious goal then attention must be paid to the physical, social, service, business and professional environments in which the informal carer operates.

6.3.5 Lessons learned: general lessons learned

The epidemiologic study of people who are exposed to providing informal care exposed some important methodological issues. To begin with, the epidemiological study of informal care epidemiology requires separation of the person who provides the care (the carer) and the behavioural act of care (the provision of what is necessary for the health, welfare, maintenance, and protection of another individual). This is because many people who provide care may not associate with the term or recognise themselves as a 'carer'. This became evident when recruiting for the GCCS, although the terms 'caregiver' or 'carer' were never used during the recruitment process, some potential subjects raised the fact that they did not consider themselves to be a 'carer' but rather they were performing the duties of for example a spouse, sibling or child of. On a similar vein, the identification of a 'carer' is not necessarily the same as identifying an individual who is actively involved in providing care to another who is sick, elderly or disabled. This was a problem across all the studies included in the two systematic reviews. However, it was particular problem for some of the studies included in the intervention review, where many studies reported high levels of drop out. Reasons for high levels of drop out included intervention perceived not to be relevant.

6.4 The structure, purpose, limitations, use and misuse of the informal care epidemiological literature

Although the discipline of epidemiology is not generally recognised as a framework for the study of people who provide informal care, many epidemiological concepts and methods are used in studies of informal carers. Moreover, it is relatively easy to view informal care from an epidemiological perspective; provision of informal care is a behaviour which is exogenous to and not necessary for the normal functioning of the individual providing the informal care, and is a potential causal characteristic in that exposure to informal care may alter the pattern of disease and health.

With this in mind, the discipline of epidemiology offers a body of principles with which to design and evaluate studies and to determine the reliability and utility

of study findings which is worth exploring and maybe of benefit to those who wish to undertake research on informal carers in the future.

6.4.1 The structure of the informal care epidemiological literature

6.4.1.1 Informal carers, a special population ‘exposed’ to stress

Over the last thirty years ‘carers’ have been considered and studied in a number of studies as what may be termed a ‘special exposure cohort’⁴³⁷, that is an identifiable group with an exposure to an agent of interest, in this case stress as a consequence of providing care to someone in ill health, disability or frailty. Indeed studies of people who provide care have been described as ‘a natural experiment of the health consequences of extreme, chronic stress, allowing researchers to examine not only mental health outcomes, such as depression but also the correlates of those outcomes.’⁶⁶ One early example of using carers as a ‘special exposure cohort’ is a study which includes a group of forty-four people who provide care to spouses with a diagnosis of Alzheimer’s disease⁴⁵³. Fiore reports that this group of people were chosen as the subjects of this study as they provided a ‘stressed subject population considered at high risk for depression.’ A more recent study conducted by Kiecolt-Glaser⁴⁴² used ‘spousal dementia caregivers’, to study the relationship between chronic stress, as a consequence of providing care to spouses with a diagnosis of Alzheimer’s disease, and the production of a specific proinflammatory cytokine, interleukin-6 (IL-6). Proinflammatory cytokines are linked to increased mortality and morbidity.

6.4.2 Types of epidemiological activity in the informal care-giving literature

There are two different types of epidemiological activity in the informal care-giving literature: descriptive and causal inference.

6.4.2.1 Descriptive studies

Descriptive studies are by far the most frequent type of epidemiological activity found in the informal care-giving published literature. With descriptive studies,

the primary aim is often to describe the distributions of adverse health outcomes in care-giving populations. The epidemiological measure of interest is usually either the occurrence of an event, such as incidence or prevalence, or an outcome measured on for example a standardised rating scale. Often these descriptive studies will include an analytic element in that they will assess for example whether two variables are associated, the influence several variables on one variable or to enable the prediction of one value from another.

One of the earliest published epidemiological studies on the relationship between informal care and adverse health outcomes in populations was Brocklehursts paper on 'The social effects of stroke'⁴⁴³. In this paper, Brocklehurst reports that during the year of follow-up 'the number of chief carers who regarded their health as poor' rose from n = 10 to n = 28) and the proportion receiving medical treatment increased from 33% at the first study visit to 40% at 12 month follow-up. This study provides the first indication that there may be a relationship between providing care to stroke survivors and the development of ill health.

6.4.2.2 Causal inference

The second type of epidemiological endeavour in the informal carer literature causal inference, the purpose of which is to estimate the 'effect' of the potential causal factor or 'exposure' on the occurrence of one or more health related outcomes (effect). The effect of interest is the change in population health outcome-frequency measures, such as incidence proportion or rate brought about by an 'exposure' being at one level or another²¹⁰. In the informal care-giving literature, 'exposure' can refer to informal care as a behaviour, that is behaving in such a way as to provide what is necessary for the health, well-being, maintenance or protection of another in ill health, frailty or disability. Equally, 'exposure' in the informal care literature can also refer to an intervention such as an educational⁶³ or support group intervention³²⁰ or exposure can refer to a 'health state' such as carer strain (exposure) (in people who provide care) as a cause of death (outcome)²⁹.

Therefore in informal care epidemiology, the characteristic which defines the group can be:

- a behaviour (that is behaving in such a way as to provide what is necessary for the health, well-being, maintenance and protection of someone in ill health, frailty or disability)
- a health state (carer strain, depression, anxiety) in those behaving in such a way as to provide what is necessary for the health, well-being, maintenance and protection of someone in ill health, frailty or disability (behaviour).
- a therapeutic intervention (education, counselling) delivered to those behaving in such a way as to provide what is necessary for the health, well-being, maintenance and protection of someone in ill health, frailty or disability (behaviour).

6.4.2.2.1 *Informal care as a behaviour*

Determining the change in health outcome frequency measures (effect) of the provision of informal care (behaviour) brought about by the informal care exposure being at one level versus another activity is quite rare in the informal care-giving literature. However, there are some examples including Hirsts⁵⁰ population based study on carer psychological distress from the British Household Panel Survey. From this work, it is possible to say that for people who provide informal care (a behaviour), the effect of providing informal care for 20+ hours per week compared to not providing care at all is to increase the odds of psychological distress (OR 2.86, 95% CI 2.09 - 3.91, $p < 0.001$), that is the odds of psychological distress in those exposed to providing care is approximately 200% higher than those individuals not exposed to providing care⁵⁰.

Another example is Kiecolt-Glaser's study⁴⁴² of the change in levels of IL-6 brought about by informal care activity being at one level or another i.e., exposed to care-giving versus not exposed to care-giving. Esterlings⁴⁵¹ study provides another example of changes in perceived stress, depression and natural killer cell response to recombinant interferon- γ and recombinant interleukin-2 stimulation in vitro brought about by informal care being at one level or another i.e., continuing or current carer versus former carer versus non-care giver.

Simons²⁵⁸ cohort study of informal carers of stroke survivors which compared live-in carers to a non-carer group to estimate the depressive effects of providing care provides yet another illustration the change in health outcome measures brought about by informal care-giving exposure levels being at one level or another. However, there were a number of limitations in the design of this study therefore the results have to be viewed with caution.

6.4.2.2.2 *An intervention delivered to a cohort of informal carers*

Determining the change in health outcome frequency measures (effect) of an intervention delivered to a cohort of informal carers (who have the experience of providing informal care to someone in ill health, frailty or disability in common) brought about by the intervention (exposure) being at one level versus another activity is common in the informal care-giving literature. The most common example of this kind of activity is the clinical trial. If the 'exposure' is a therapeutic intervention such as an educational⁶³ or support group intervention³²⁰ then it is possible to say that for people who provide informal care, the effect of an intervention (such as an educational programme on how to support and care for stroke survivors compared to no educational programme at all) is to reduce the risk of care-related strain.

6.4.2.2.3 *A cohort of informal carers where the exposure is a health state*

Determining the change in health outcome frequency measures (effect) brought about by a health state being at one level or another in a cohort of informal carers (who have the experience of providing informal care to someone in ill health, frailty or disability in common) is relatively rare in the informal care-giving literature.

So for example in the Schulz study²⁹, the study population were categorised by the level of care they provided and by level of self-reported carer strain, where 'exposure' is a 'health state' in this example, carer strain. In this example it is possible to say that for people who provide care to ill or disabled spouses and report being strained (where strain is the health state or 'exposure'), the effect of being strained compared with providing care and not being under strain is to increase the risk of four year all cause mortality²⁹.

6.4.3 Methodological issues in epidemiological study of informal carers

6.4.3.1 Natural assignment versus random allocation

When the exposure is behaviour (such as informal care) or a health state (such as stress) then there is natural assignment of the exposure level (as opposed to random allocation), therefore the assignment occurs naturally without intervention from investigators. This natural assignment may be based on unknown or unmeasured attributes of individuals which can lead to substantial confounding and difficulty drawing causal inferences. In contrast, random allocation gives each participant an equal chance of being allocated to a different level of exposure (such as an education programme on how to care for and support stroke survivors) the aim of which is to ensure that known and unknown participant characteristics are equally distributed between the intervention and comparator groups, thereby attempting to eliminate selection bias.

6.4.3.2 Methodological issues specific to the epidemiological study of informal carers

The epidemiological study of informal carers is complicated by some important methodological problems which must be taken into consideration in future research. The main issues are outlined below.

- There is no widely accepted clear, unambiguous definition of the informal care exposure. The lack of a detailed definition of a current informal carer (in stroke or any other disease state which can cause disability) makes it difficult to work out the true informal care exposure prevalence and therefore to obtain a valid and precise estimate of the frequency (incidence rate or proportion) of disease or ill health in those who have been truly exposed. In addition, lack of a clear definition is a major problem in selecting participants for, designing interventions for and applying the results of, randomised controlled trials testing interventions directed towards informal carers.

- The interpretation of epidemiological data of informal care exposure and outcomes of interest depends directly on the validity of the methods used to measure the informal care exposure. To date, there is a dearth of valid methods (self-report questionnaire, personal interview, diary, observation by investigator) for the measurement of the informal care exposure.
- Informal care is a chronic exposure. Individuals may experience various levels of exposure (for example hours care provided per week), which may change over time and follow no particular pattern.
- Currently, there is no guidance on where to draw the boundary between being exposed to informal care and unexposed. With a few exceptions the majority of individuals have a natural tendency to ‘care for, defend, share resources with, warn of danger, or otherwise show altruism towards’^{438;439} others. The question is what features distinguish what is our innate predisposition to promote the welfare of another individual from providing what is necessary for the health, welfare, maintenance or protection of another individual in ill health, frailty or disability.

6.4.4 Limitations of the informal care epidemiological literature

6.4.4.1 Issues involving understanding or correct interpretation of epidemiological concepts and methods in the literature

Misunderstandings involving measures of occurrence although rare in the informal carer literature can lead to confusion about what measures of effect can be calculated from measures of occurrence, what this means and how the results from the study are used in the wider context.

One systematic review⁴⁴⁴ of depressive disorders in carers of dementia patients uses prevalence data to calculate the relative risk. Relative risk or risk ratio is calculated from the incidence proportion under condition ‘exposed’ and condition ‘unexposed’, not from prevalence data. This systematic review also refers to calculating incidence rates for each of the prospective studies included in the review and goes on to describe the proportions of people assessed as or

reporting depressive symptoms at follow-up, relative to baseline. Incidence rates measure the occurrence of new cases of depression per unit of person time and would usually involve incidence time and hazard models to model the average time to the occurrence of the event, in this case depression.

Depression is a recurrent condition and therefore is likely to involve time-varying covariates (such as health care interventions including medication and therapy, the seasons, a persons activity level). In the informal care-giving situation the outcome (depression) may affect (as well as be affected by) the informal care exposure. For example, signs and symptoms of depression may include fatigue and decreased energy levels may influence an informal carers ability to perform informal care-giving activities over several days; furthermore, a previous episode of depression may directly affect the risk of the next depressive episode.

Therefore, careful consideration has to be given to the best way to handle rates of recurrent depression events and how to analyse them.

6.4.5 Use and misuse of the informal care epidemiological literature

6.4.5.1 The science beneath the spin

“Statistics are like a drunk with a lamppost: used more for support than illumination.”

Winston Churchill

People and organizations can manipulate information for their own purposes. Therefore, it is vital to discover what methods were used to collect and analyse the data.

For example a recent headline on the BBC Health website states, ‘Elderly carers need more support from GPs’⁴⁴⁵. The article goes on to say that ‘almost 70% of hundreds of older carers questioned in a survey said that their health was suffering because of their (care-giving) responsibilities’. The source of the data was a report produced by the Princess Royal Trust for Carers, a very credible charitable body. In their report⁴⁴⁶, the Princess Royal Trust for Carers make recommendations which include GPs screening carers for depression at least once a year and the need for all services which support carers to be aware of

the poor mental health often experienced by informal carers. These recommendations are supported by the Royal College of General Practitioners⁴⁴⁵.

A closer look reveals that this information was generated from a simple Web-based survey of a convenience sample of 639 older carers. Web-based surveys are subject to three types of bias or ‘error’: coverage bias, selection bias and measurement error. Therefore, the results of this survey should be viewed with caution.

6.4.5.2 Don’t let the facts get in the way of a good story

Every day, we are bombarded by facts and figures in the media. The news often quotes facts and figures related to informal carers, the majority of which originate from primary research studies; although the information from these studies can be valid and reliable, it is interesting to see how different forms of media spin the findings.

For example a recent headline in the Nursing-Times.net warns of a ‘cancer patient carer depression risk’⁴⁴⁷. This headline was generated from a survey of a sample of patient care-dyads admitted to one of two hospices⁴⁴⁸. The study found that 38% of caregivers had CES-D 10 scores of 4 or greater, predictive for a diagnosis of depression, upon patient admission to hospice. The original article recommends that caregivers are screened for depression when cancer patients enter the hospice environment. From an individuals perspective, a score of 4 or greater may identify symptoms of major depressive disorder which may need to be addressed, but from an epidemiological perspective a depression prevalence of 38% does not indicate a causal relationship between either exposure to providing care to people with terminal cancer or hospice entry and depression. An apparently high prevalence does not equate with increased risk.

6.4.5.3 Always check the source reference

A clinical review article entitled ‘Depression in older adults’⁴⁴⁹ published in the British Medical Journal (BMJ), the authors list ‘being a carer’ as one of nine psychosocial risk factors for depression in older people. The authors reference a review article by Colasanti et al⁴⁵⁰ as the source of their information on risk

factors for depression in older people. Closer inspection of the article by Colasanti reveals no evidence of or no reference to older people providing care as a risk factor for depression. When journals such as the BMJ, a highly respected medical journal with a wide readership, prints information which is not substantiated by well reasoned supporting evidence then it is easy to see how the assertion that being a carer is a risk factor for depression, can become orthodoxy without being accurate. It is also easy to see how this kind of assertion becomes received wisdom by virtue of bona fide medical journal endorsement.

6.4.6 The structure, purpose, limitations, use and misuse of the informal care epidemiological literature: conclusions

Informal care epidemiology encompasses a wide range of topics, from the study of the distributions and determinants of ill health in care-giving populations, to the study of the effects of exposure to providing care on the occurrence of adverse health outcomes, to clinical trials of therapeutic interventions targeted towards informal carers.

While it is difficult to control how the findings from research is interpreted by outside agencies, there is much that can be done by researchers to increase the validity and reliability of their findings.

6.5 Recommendations for research, clinical practice and policy

6.5.1 Recommendations for future research

1. To update the non-pharmacological interventions review to include the 11 randomised controlled trials that are currently ongoing.
2. To look beyond the informal carer as someone who needs to be 'changed' in some way (knowledge, skills, abilities) to preserve their health and look instead to the physical and social environment in which they operate for ideas and

inspiration for research. For example, a programme training health and social care professionals on the role and function of informal carers of stroke survivors.

3. For epidemiological studies of people who provide informal care:

- The development of a substantively meaningful conceptualization of the informal care exposure.
- The creation of an operational definition of the informal care exposure which can be easily measured⁴⁴⁰.
- Consider the most effective way to categorise the informal care exposure as it relates to adverse health outcome causation⁴⁴⁰.
- Consider the most critical time period during which the informal care exposure is most likely to cause adverse health outcomes⁴⁴⁰.
- Develop an algorithm to calculate the intensity of the informal care exposure variable over the time period of the study that can be used in future epidemiological studies of informal carers⁴⁴⁰.

6.5.2 Recommendations for clinical practice

Health care and social care professionals need to be aware of the high risk of stress in carers. There is insufficient information from studies of high quality to determine if there is a causal association between provision of informal care and depression. There is a general acceptance that good clinical care will include providing information, advice and informal support to carers (as well as to patients). The conclusions of this research do not provide any clear evidence on how best to perform these roles.

6.5.3 Recommendations for policy

Carers are recognised as playing a vital role in supporting family members who are sick, infirm or disabled⁴⁵².

In a very direct sense, people who provide informal care to those in ill health, frailty or disability will benefit or suffer from government policy initiatives. While 'informal carers' are not a controversial policy area, it is important that the benefits that the 'informal carers' group receive from government are fair, relevant and justifiable.

Therefore, the key recommendation for policy makers is to be very clear on what is meant by 'informal carer', or 'unpaid carer' or 'caregiver' as these terms mean different things to different people. On the other hand, while clear unambiguous definitions are vital for good science, it is recognised that a certain vagueness around the term 'informal carer' may be necessary and advantageous in politics.

Ideally, effective public policy should be developed on the basis of valid and reliable information from studies of high quality. Policy makers should take care to ensure that real and important risks are distinguished from spurious or imagined risks and epidemiologists can assist policy makers in making this distinction. Equally, policy makers should be aware of the evidence of the effects of interventions from, for example Cochrane systematic reviews, the gold standard of reviews. Combined, this should pave the way for rational allocation of intervention resources.

Policy makers should look beyond the informal carer for opportunities and ideas for improvement which would assist informal carers to function efficiently and effectively. For example, the provision of accurate drug prescriptions and medical staff who are responsive to information from carers (such as information on drug allergies) would help towards reducing stress.

Finally, policy makers should be aware that not all scientific information is valid and reliable. Each piece of scientific information should be carefully assessed to judge its trustworthiness, relevance and utility. Bona fide credentials of the organisation producing the evidence do not guarantee scientific rigour or quality.

Appendices

**APPENDIX 1: THE GLASGOW CARERS COHORT STUDY FULL
STUDY INFORMATION FOR POTENTIALLY EXPOSED PARTICIPANTS**



University
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Study Title: The Glasgow Carers Cohort Study: A study on the effects of providing care to stroke survivors.

Principal Investigators:

Lynn Legg, Research Training Fellow
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10 Alexandra Parade
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Funder: Chief Scientist Office (CSO), the Scottish Government.

Invitation to Participate

You are being invited to participate in a research study as a partner or relative or friend of a patient who has been admitted to the Stroke Service at Glasgow Royal Infirmary with a stroke. To join this study is voluntary. You may refuse to join, or you may withdraw your consent to be in the study, for any reason. By reading this information and signing the consent form (attached to this document) you are indicating your willingness to participate in this study. Once you have signed the consent form you will be asked to complete an eligibility screening questionnaire to gather information about your past medical history and any existing care giving commitments that you have to family members, friends, neighbours or others because of long-term physical or mental ill health or disability, or problems related to old age. After you have completed these questions, the investigators can decide if you are a candidate for this study and you will be contacted by telephone or in person and given further instructions at that point.

Research studies are designed to obtain new knowledge that may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies.

Deciding not to be in the study or leaving the study before it is finished will not affect your relationship with the researcher, your health care provider or the University of Glasgow. It will also have no impact on the person that you care for, the health service they receive or the amount of time that they will spend in hospital.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study. You should ask the researchers named above any questions that you have about this study at any time.

Why are we doing this study?

One in ten of the UK population provides help and support to family members, friends, neighbours or others because of: long-term physical or mental health ill health or disability, or problems related to old age. This informal caring network provides a huge benefit to society by preventing people going into costly care homes. Stroke is a major cause of adult disability and at any one time 0.5% of the UK population are dependent as the result of a stroke. Much of the burden of providing for the needs of these people falls to the informal carer often a family member or close friend. Providing help and support to a stroke survivor can be hard, and can sometimes lead to stress.

We would like to follow-up a group of people who look after, help or provide support to stroke survivors. As every stroke survivor is unique, we expect that the people providing care will have a different experience, for example in the amount of care that they have to provide or the kinds of activities that they have to help with.

The purpose of doing this study is to assess the effects of looking after, helping or providing support to stroke survivors on the health of the person who is providing the care. We are also interested to find out what 'carer', stroke survivor and 'care' characteristics influence why some carers fair better than others.

Who should participate?

- Are you aged over sixteen?

Are you a partner or relative or friend of a patient who has been admitted to the Stroke Unit at Glasgow Royal Infirmary?

Will you look after, or give help and support to the stroke survivor when they return home with you or return to their own home (not a hospital, long-term care facility, residential facility or nursing home)?

If you answered yes to these questions, please read on before making you decision to participate in the study.

What will happen during the study?

First, the principal investigator (Lynn Legg) will review the study protocol and potential risks and benefits of the study with you. Then, you will be asked to complete a series of more in-depth questionnaires. We will ask you to complete the first main questionnaire before the person (stroke survivor) that you will look after; help or support leaves hospital and returns home. We will then ask you to complete further questionnaires at three months and six months. These questionnaires will ask you a series of questions relating to your health and well-being, the help you get from friends and family and your care giving responsibilities. We will also collect information on the person (stroke survivor) that you look after, help or support but we will collect this information from the hospital notes.

When will I do this?

You will be asked to complete a questionnaire when you enter the study, then three months and six months later.

How long will it take me?

Each questionnaire will take on average 25 minutes to complete.

What will happen?

We hope to be able to work closely with each person who has agreed to take part in the study. We will arrange with you the most suitable and convenient way for you to complete the questionnaires. This may be in person with the study researcher, by telephone or by post.

If you choose to complete the questionnaires with the study researcher you can choose a venue and a time which is most convenient for you, for example at home, or at a stroke clinic. If you choose to complete the questionnaire by telephone we will again arrange a time that suits you. If you choose to return the questionnaires by post we will provide you with a stamped addressed envelope.

We understand that everyone has very busy lives therefore our aim is to make participation in this study as simple, quick and convenient as possible.

How many people will take part in this study?

We are hoping to recruit 115 carers and 115 non-care giving people.

How will your privacy be protected?

The information contained in each of the questionnaires will be entered into a computer package, which will allow the data to be analysed. At all times electronic data (that is, information stored electronically on computer drives and disks) will remain in password-protected computer files. Paper copies, including completed questionnaires, will be stored in locked filing cabinets. Carer contact information and survey data will be stored in separate locations and/or computer files whenever possible. To further protect the identity of the study participants, each person participating in a study will be assigned a subject number, which will be used whenever possible instead of that person's name.

Identifiable study data will only be transported between sites (for example, from the Academic Section of Geriatric Medicine, Glasgow Royal Infirmary to Robertson Centre for Statistics, University of Glasgow) using email with highly secure encryption technology.

Will there be potential harm during the study?

While we have made every attempt to make the questionnaires as unobtrusive as possible we realize that some of the questions may be quite personal in nature. If you feel at all uncomfortable answering any of the questions, you are free to skip a question and move to the next one.

Once you have completed a questionnaire, you might feel like you would like to talk to a member of the Glasgow Royal Infirmary Stroke Service. If this does happen, then the researcher will discuss with you the available options.

Will information from the study be given to my GP?

We will write a letter to your GP to tell them that you are involved in this study.

What are the benefits if I participate in the study?

There may be no direct benefits to you personally for participating in this study. However, the information will help us to understand the impact of providing care to stroke survivors. It will also enable us to develop ways of identifying carers who would benefit from extra help and also to find out what kind of specific services, activities or products should be developed in the future.

Who will know what I said in the questionnaires?

Lynn Legg, Principal Investigator will administer and collect the questionnaires and enter the questionnaire responses onto a computer package. Lynn Legg and

Professor Peter Langhorne, the principal investigators, will analyse the data, however, your name will not be attached to the data being analysed. The findings will be included in a report to the Chief Scientist Office, Scotland and will also form the basis of a PhD thesis. We also expect that the study results will be published in stroke specific and general medical journals as well as presented at national and international conferences. Again, personal information or other identifying information will not be included in any reports. Your personal information collected in this form is for this research project only. This information will be kept in confidence. This information will not be used for any other purpose or disclosed without your consent.

What if I change my mind about participating in the study?

Your participation is voluntary. You may decide to withdraw from the study at any time with no further consequence to you. Your decision will not affect the health care that is provided to the person that you care for or increase their length of stay in hospital.

Will I have access to the final report?

The written report of the study will be available to you if you wish.

Who do I contact to participate or for more information?

If you have questions about this project, please call:

Lynn Legg
Research Fellow
Academic Section of Geriatric Medicine
Room 34, Level 3, University Block
Queen Elizabeth Building
10 Alexandra Parade
Glasgow Royal Infirmary University NHS Trust
Glasgow G31 2ER
Tel +44 (0) 141 211 495

APPENDIX 2: THE GLASGOW CARERS COHORT STUDY

CONSENT FORM FOR EXPOSED PARTICIPANTS

Telephone: 0141 211 4976

Date:

Academic Section of Geriatric Medicine
3rd Floor University Block
Royal Infirmary
Alexandra Parade
Glasgow, G31 2ER

Centre Number:



CARER CONSENT FORM

Title: The Glasgow Carers Cohort Study

Name of Researchers: Lynn Legg and Peter Langhorne
Academic Section of Geriatric Medicine, 3rd floor University Block, Royal
Infirmary, Glasgow, G31 2ER. Telephone: 0141 211 4953

Please initial box

1. I confirm that I have read and understand the information sheet for the above study and have had the opportunity to ask questions.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
3. I agree to continue to take part in the above study.

Name of Carer	Date	Signature
Name of Person taking consent (if different from researcher)	Date	Signature
Researcher	Date	Signature

**APPENDIX 3: THE GLASGOW CARERS COHORT STUDY
SCREENING FORM FOR EXPOSED PARTICIPANTS**

5. Will you provide most of the care for the stroke survivor when they return home with you or return to their own home (i.e. not a hospital, long-term care facility, residential facility or nursing home)?

- Yes
- No
- Not sure

6. Will the stroke survivor live with you?

- Yes
- No, they will live somewhere else
- Not sure

7. Did you look after, or give help or support to (*stroke survivor's name*) because of: long-term physical or mental ill-health or disability, or problems related to old age before this admission to hospital?

- No
- Yes, 1-19 hours a week
- Yes, 20-49 hours a week
- Yes, 50+ hours a week

8. Do you look after, or give help or support to any other family members, friends, neighbours or others because of: long-term physical or mental ill-health or disability, or problems related to old age?

- No
- Yes, 1-19 hours a week
- Yes, 20-49 hours a week
- Yes, 50+ hours a week

CHRONIC HEALTH CONDITIONS

We are interested in any chronic health conditions that you may have. We are interested in 'long-term conditions' that have or are expected to last more than 6 months and that have been diagnosed by a doctor.

1. Has your doctor every told you that you have:
/ All boxes that apply

- *Cirrhosis or liver disease
- *Diabetes
- *Eye, kidney or nerve damage due to diabetes

There are many other health products such as ointments, vitamins, herbs, minerals or protein drinks which people use to prevent illness or to improve or maintain their health.

2. In the past month, have you used any ointments, vitamins, herbs, minerals or protein drinks?

Yes
No

Can you please list the ointments, vitamins, herbs, minerals or protein drinks that you have taken over the last month.

Thank you!

**APPENDIX 4: THE GLASGOW CARERS COHORT STUDY
EXPOSED PARTICIPANT BASELINE QUESTIONNAIRE**



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SECTION 1: NAME AND ADDRESS

1. What is your name?
2. What is your address?
3. Post code?
4. What is your telephone number? (In case we need to contact you)
5. What is your mobile telephone number (In case we need to contact you)

SECTION 2 GENERAL PRACTITIONER (GP) DETAILS

1. What is your GPs name?
2. What is your GPs address?
3. What is your GPs telephone number?

SECTION 3: ABOUT YOU

1. What is your sex? (Please circle one)

Male Female

2. What is your date of birth?

--	--	--	--	--	--	--	--

3. What is your marital status? (Please tick)

Single
 Married
 Separated or divorced
 Widowed

4. What is your relationship to.....

(Please tick)

- Husband or wife
- Partner
- Son or daughter
- Step-child
- Brother or sister
- Mother or father
- Step-mother o step father
- Grandchild
- Grand-parent
- Other related
- Unrelated

ETHNIC GROUP

5. What is your ethnic group? (Please circle)

1. White

Scottish
 Other British
 Irish
 Other white background

2. Mixed

Any mixed background

3. Asian, Asian Scottish or Asian British

Indian
 Pakistani
 Bangladeshi
 Chinese
 Other Asian background

4. Black, Black Scottish or Black

British
 Caribbean
 African
 Other black background

5. Other ethnic background

EMPLOYMENT

If you are aged 16-74 please complete go to Question 6.

If you are age 75 and over please go to Question 8.

Last week were you doing any work:

as an employee?
 as self-employed/ freelance?
 in your own family business? or
 on a government training scheme?

‘Yes’, if you were away from work ill, on maternity leave, on holiday or temporarily laid off.

'Yes' for any paid work including casual or temporary work, even if only for one hour.

'Yes', if you worked paid or unpaid, in your own / family business

'Yes', go to question 8

'No', go to question 7

7. Last week were you any of the following? (Please circle)

Retired

Student

Looking after home/ family

Permanently sick/ disabled

None of the above

Go to question 9 'Qualifications'.

8. How many hours (to the nearest full hour) a week do you usually work in your main job?

Give average for last 4 weeks

Number of hours worked a week

QUALIFICATIONS

9. Which of these qualifications do you have?

/ All boxes that apply

- 'O'Grade, Standard Grade, Intermediate 1, Intermediate 2, GCSE, CSE, Senior Certificate or equivalent
- Higher Grade, CSYS, Scottish Group Award at higher, 'A' Level, AS Level, Advanced Senior Certificate or equivalent
- GSVQ/SVQ Level 1 or 2, SCOTVEC/National Certificate Module, BTEC First Diploma, City and Guilds Craft, RSA Diploma or equivalent
- GSVQ/SVQ Level 3, ONC, OND, SCOTVEC National Diploma, City and Guilds Advanced Craft, RSA Advanced Diploma or equivalent
- First Degree, Higher Degree
- Professional Qualifications (for example teaching, accountancy)
- None of these

SECTION 4: ABOUT YOUR GENERAL HEALTH

1. In general, would you say that your health is: (please circle one)

Excellent
Very good
Good
Fair
Poor

2. Compared to one year ago, how would you rate your general health now?
(Circle one number)

- 1 Much better than one year ago
- 2 Somewhat better than one year ago
- 3 About the same as one year ago
- 4 Somewhat worse than one year ago
- 5 Much worse than one year ago

The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? (Circle one number)

3. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports.

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

4. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf.

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

5. Lifting or carrying groceries.

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

6. Climbing several flights of stairs

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

7. Climbing one flight of stairs

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

8. Bending, kneeling, or stooping

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

9. Walking more than a mile

- 4 Yes, limited a lot
- 5 Yes, limited a little
- 6 No, not limited at all

10. Walking several hundred yards

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

11. Walking one hundred yards

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

12. Bathing or dressing yourself

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

(Circle yes or no)

13. Cut down the amount of time you spent on work or other activities

Yes No

14. Accomplished less than you would like

Yes No

15. Were limited in the kind of work or other activities

Yes No

16. Had difficulty performing the work or other activities (for example, it took extra effort)

Yes No

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

(Circle yes or no)

17. Cut down the amount of time you spent on work or other activities

Yes No

18. Accomplished less than you would like

Yes No

19. **Didn't do work or other activities as carefully as usual**

Yes No

20. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups? (Circle one number)

- 1 Not at all
- 2 Slightly
- 3 Moderately
- 4 Severe
- 5 Very severe

21. How much bodily pain have you had during the past 4 weeks?

- 1 None
- 2 Very Mild
- 3 Mild
- 4 Moderate
- 5 Severe
- 6 Very severe

22. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

- 1 Not at all
- 2 A little bit
- 3 Moderately
- 4 Quite a bit
- 5 Extremely

These questions are about how you feel and how things have been with you during the last 4 weeks. For each question, please give the answer that comes closest to the way you have been feeling.

23. Did you feel full of pep?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

24. Have you been a very nervous person?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

25. Have you felt so down in the dumps that nothing could cheer you up?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time

6 None of the time

26. Have you felt calm and peaceful?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

27. Did you have a lot of energy?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

28. Have you felt downhearted and blue?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

29. Did you feel worn out?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

30. Have you been a happy person?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time

6 None of the time

31. Did you feel tired?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

32. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

(Circle one number)

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

How true or false is each of the following statements for you?

(Circle one number)

33. I seem to get sick a little easier than other people

- 1 Definitely true
- 2 Mostly true
- 3 Don't know
- 4 Mostly false
- 5 Definitely false

34. I am as healthy as anybody I know

- 1 Definitely true
- 2 Mostly true
- 3 Don't know
- 4 Mostly false
- 5 Definitely false

35. I expect my health to get worse

- 1 Definitely true
- 2 Mostly true
- 3 Don't know
- 4 Mostly false
- 5 Definitely false

36. My health is excellent

- 1 Definitely true
- 2 Mostly true
- 3 Don't know
- 4 Mostly false
- 5 Definitely false

SECTION 5: HOW YOU FEEL

On the next page are a number of statements about your well being. Would you please indicate how much you agree or disagree by circling number beside the statement you have picked.

1. I don't feel particularly pleased with the way I am

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

2. I feel that life is very rewarding

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

3. I am well satisfied about everything in my life

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree

6 Strongly agree

4. I don't think I look attractive

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

5. I find beauty in some things

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

6. I can fit in everything I want to

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

7. I feel fully mentally alert

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

8. I do not have particularly happy memories of the past

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree

6 Strongly agree

This section consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the **one statement** in each group that best describes the way you have been feeling during the past two weeks, including today. Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (Changes in Sleeping Pattern) or Item 18. (Changes in Appetite).

1. Sadness

- 1 I do not feel sad.
- 2 I feel sad much of the time.
- 3 I am sad all the time.
- 4 I am so sad or unhappy that I can't stand it.

2. Pessimism

- 1 I am not discouraged about my future.
- 2 I feel more discouraged about my future than I used to be.
- 3 I do not expect things to work out for me.
- 4 I feel my future is hopeless and will only get worse.

3. Past Failure

- 1 I do not feel like a failure.
- 2 I have failed more than I should have.
- 3 As I look back, I see a lot of failures.
- 4 I feel I am a total failure as a person.

4. Loss of Pleasure

- 1 I get as much pleasure as I ever did from the things I enjoy.
- 2 I don't enjoy things as much as I used to.
- 3 I get very little pleasure from the things I used to enjoy.
- 4 I can't get any pleasure from the things I used to enjoy.

5. Guilty Feelings

- 1 I don't feel particularly guilty.
- 2 I feel guilty over many things I have done or should have done.
- 3 I feel quite guilty most of the time.
- 4 I feel guilty all of the time.

6. Punishment Feelings

- 1 I don't feel I am being punished.
- 2 I feel I may be punished.
- 3 I expect to be punished.
- 4 I feel I am being punished.

7. Self-Dislike

- 1 I feel the same about myself as ever.
- 2 I have lost confidence in myself.
- 3 I am disappointed in myself.
- 4 I dislike myself.

8. Self-Criticalness

- 1 I don't criticize or blame myself more than usual.
- 2 I am more critical of myself than I used to be.
- 3 I criticize myself for all of my faults.
- 4 I blame myself for everything bad that happens.

9. Suicidal Thoughts or Wishes

- 1 I don't have any thoughts of killing myself.
- 2 I have thoughts of killing myself, but I would not carry them out.
- 3 I would like to kill myself.
- 4 I would kill myself if I had the chance.

10. Crying

- 1 I don't cry anymore than I used to.
- 2 I cry more than I used to.
- 3 I cry over every little thing.
- 4 I feel like crying, but I can't.

11. Agitation

- 1 I am no more restless or wound up than usual.
- 2 I feel more restless or wound up than usual.
- 3 I am so restless or agitated that it's hard to stay still.
- 4 I am so restless or agitated that I have to keep moving or doing something.

12. Loss of Interest

- 1 I have not lost interest in other people or activities.
- 2 I am less interested in other people or things than before.
- 3 I have lost most of my interest in other people or things.
- 4 It's hard to get interested in anything.

13. Indecisiveness

- 1 I make decisions about as well as ever.
- 2 I find it more difficult to make decisions than usual.
- 3 I have much greater difficulty decisions than I used to.
- 4 I have trouble making any decisions.

14. Worthlessness

- 1 I do not feel I am worthless.
- 2 I don't consider myself as worthwhile and useful as I used to.
- 3 I feel more worthless as compared to other people.
- 4 I feel utterly worthless.

15. Loss of Energy

- 1 I have as much energy as ever.
- 2 I have less energy than I used to have.
- 3 I don't have enough energy to do very much.
- 4 I don't have enough energy to do anything.

16. Changes in Sleeping Pattern

0. I have not experienced any change in my sleeping pattern
- 1a I sleep somewhat more than usual.
- 1b I sleep somewhat less than usual.
- 2a I sleep a lot more than usual.
- 2b I sleep a lot less than usual.
- 3a I sleep most of the day
- 3b I wake up 1-2 hours early and cannot get back to sleep.

17. Irritability

- 1 I am no more irritable than usual.
- 2 I am more irritable than usual.
- 3 I am much more irritable than usual.
- 4 I am irritable all the time.

18. Changes in Appetite

- 0 I have not experienced any change in my appetite.
- 1a My appetite is somewhat less than usual.
- 1b My appetite is somewhat greater than usual.
- 2a My appetite is much less than before.
- 2b My appetite is much greater than usual.
- 3a I have no appetite at all.
- 3b I crave food all the time.

19. Concentration Difficulty

- 1 I can concentrate as well as ever.
- 2 I can't concentrate as well as usual.
- 3 It's hard to keep my mind on anything for very long.
- 4 I find I can't concentrate on anything.

20. Tiredness or Fatigue

- 1 I am no more tired or fatigued than usual.
- 2 I get more tired or fatigued more easily than usual.
- 3 I am too tired or fatigued to do a lot of the things I used to do.
- 4 I am too tired or fatigued to do most of the things I used to do.

21. Loss of Interest in Sex

- 1 I have not noticed any recent change in my interest in sex.
- 2 I am less interested in sex than I used to be.
- 3 I am much less interested in sex now.
- 4 I have lost interest in sex completely.
- 5 Not applicable

SECTION 5: HOW YOU ARE COPING

These questions about your feelings and thoughts during the last month. In each case, please circle the number that indicates how often you felt or thought a certain way.

1. In the last month, how often have you been upset because of something that happened unexpectedly?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

2. In the last month, how often have you felt that you were unable to control the important things in your life?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

3. In the last month, how often have you felt nervous and "stressed"?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

4. In the last month, how often have you felt confident about your ability to handle your personal problems?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

5. In the last month, how often have you felt that things were going your way?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

6. In the last month, how often have you found that you could not cope with all the things that you had to do?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

7. In the last month, how often have you been able to control irritations in your life?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

8. In the last month, how often have you felt that you were on top of things?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

9. In the last month, how often have you been angered because of things that were outside of your control?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

SECTION 5: SYMPTOMS

During the past month, how much have you been bothered by any of the following problems?

1. Stomach problems

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

2. Back pain

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

3. Pain in your arms, legs, or joints (knees, hips, etc)

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

4. Menstrual cramps or other problems with your periods (women only)

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

5. Headaches

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

6. Chest pain

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

7. Dizziness

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

8. Fainting spells

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

9. Feeling your heart pound or race

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

10. Shortness of breath

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

11. Pain or problems during sexual intercourse

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

12. Constipation, loose bowels or diarrhea

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

13. Nausea, gas, or indigestion

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

14. Feeling tired or having low energy

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

15. Trouble sleeping

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

SECTION 6: HISTORY OF DEPRESSION

The next set of questions asks about your personal medical history of depression.

2. In the past month, have you used any ointments, vitamins, herbs, minerals or protein drinks? (Please circle yes or no)

Yes

No

Can you please list the ointments, vitamins, herbs, minerals or protein drinks that you have taken over the last month?

Drug e.g. St. John's Wort, Vitamin C

SECTION 8: SMOKING

1. Have you ever smoked cigarettes at all? (Please circle yes or no)

Yes

No

2. At the present time do you smoke cigarettes daily, occasionally or not at all? (Circle one number)

1 Daily

2 Occasionally

3 Not at all

3. How many cigarettes do you smoke each day now?

None

1-14 cigarettes/day?

15-24 cigarettes/ day?

≥25 cigarettes/day

SECTION 9: ALCOHOL

1. How often do you have a drink containing alcohol for example beer, wine, spirits or any other alcoholic drink? (Circle one number)

Never

Monthly or less
Two to four times a week
Four or more times a week

2. How many drinks containing **alcohol** do you have on a typical day when you are drinking?

1 or 2
3 or 4
5 or 6
7 or 9

1 drink = ½ pint beer or 1 measure of spirit or one glass of wine

SECTION 10: OTHER WORRIES

1. Are you worried about any financial debt that you might be in?

Yes
No

Would you mind having one last check to make sure that you have answered all the questions?

**APPENDIX 5: THE GLASGOW CARERS COHORT STUDY INITIAL
LETTER OF INVITATION TO POTENTIALLY UNEXPOSED RECRUITS
FROM THE GENERAL PRACTITIONER**

Dear Patient

The Glasgow Carer's Cohort Study (GCCS)

Our practice has agreed to help with the above study and we would like to ask for your help.

Background

Providing help and support to a stroke survivor can be hard, and can sometimes lead to stress or affect a carer's health and well-being. We would like to follow-up a group of people who look after, help or provide support to stroke survivors.

We would also like to follow-up a similar group of people who **do not** look after, or give help or support to any family members, friends, neighbours or others because of: long-term physical or mental ill-health or disability, or problems related to old age.

Why are we doing this?

The purpose of doing this study is to assess the effects of looking after, helping or providing support to stroke survivors on the health of the person who is providing the care. To help us to find this out, we need to have a similar group of people **who do not** provide care to compare the carers to.

Why have I been sent a letter?

We have selected you as you are the same sex and roughly the same age as one of our carers. We call this a 'match'. At no time will you know who your 'match' is.

If I agree to take part, what will happen?

All that will happen is that you will be asked to complete a series of questionnaires at the start of the study, at 3 months and then at 6 months. Each questionnaire should take between 20 and 30 minutes to complete.

Your participation is voluntary. You may decide to withdraw from the study at any time with no further consequence to you. Your decision will not affect the health care that is provided to you.

We are hoping to recruit 115 carers over 16 years of age who provide care and 115 people who do not provide care as a comparison group.

Please return the enclosed response form in the prepaid envelope with your decision. Thank you very much for taking the time to read this invitation and I hope you will consider taking part in this interesting project.

Yours

sincerely

**APPENDIX 6: THE GLASGOW CARERS COHORT STUDY
EXPRESSION OF INTEREST FORM TO COMPLETED BY
UNEXPOSED POTENTIAL PARTICIPANTS**



University
of Glasgow



The Glasgow Carers Cohort Study: A study of the effects on informal carers of providing care to stroke survivors.

Expression of Interest

Your name: _____

Address1 _____

Address2 _____

Address3 _____

Post code _____

Please check one of the following boxes and return in the prepaid envelope

Yes, I would like to take part in this study

I would like more information before deciding

No, I would not like to take part in this study

Signature: _____

Name (print): _____

Date: _____

Tel: _____

Return address: Lynn Legg
Principal Investigator GCCS
Room 34
Academic Section of Geriatric Medicine
3rd Floor, University Block
Royal Infirmary, Glasgow, G31 2ER, UK
Email: step@clinmed.gla.ac.uk

**APPENDIX 7: THE GLASGOW CARERS COHORT STUDY
INVITATION TO POTENTIAL UNEXPOSED PARTICIPANTS**



The Glasgow Carer's
Cohort Study



University
of Glasgow



Dear Patient,

Thank you for your interest in participating in The Glasgow Carer's Cohort Study (GCCS).

Please find enclosed a formal invitation to participate in the GCCS. This provides you with more detailed information about the study and what is expected of you, if you agree to participate. If you decide that this study is not for you (once you have read all the information), please just let me know.

If you are interested, I would be very grateful if you could complete the consent form and the screening form and return them to me as soon as possible in the enclosed pre-paid envelope.

If you have any problems or concerns, or need any help, please feel free to call me on 0141 211 4953.

I look forward to hearing from you.

Best wishes

Lynn Legg,
CSO Research Training Fellow

ACADEMIC SECTION OF GERIATRIC MEDICINE
Division of Cardiovascular and Medical Science
Royal Infirmary,
3rd Fl. University Building, 10 Alexandra Parade,
Glasgow G31 2ER

Telephone: (44)-141-211-4953 Fax (44)-141-211-4033
Email: step@clinmed.gla.ac.uk

APPENDIX 8: THE GLASGOW CARERS COHORT STUDY
FULL STUDY INFORMATION FOR RECRUITMENT OF
UNEXPOSED PARTICIPANTS



The Glasgow Carer's
Cohort Study



University
of Glasgow



Study Title: The Glasgow Carers Cohort Study: A study on the effects of providing care to stroke survivors.

Principal Investigators:

Lynn Legg, Research Training Fellow
Academic Section of Geriatric Medicine
Room 34, Level 3
University Block, Queen Elizabeth Building
10 Alexandra Parade
Glasgow Royal Infirmary NHS Trust
0141 211 4953
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Professor Peter Langhorne
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Room 36, Level 3
University Block, Queen Elizabeth Building
10 Alexandra Parade
Glasgow Royal Infirmary NHS Trust
0141 211 4076
hjm2n@clinmed.gla.ac.uk

Funder: Chief Scientist Office (CSO), the Scottish Government.

Invitation to Participate

You are being invited to participate in a research study as a study 'control'. In this study, a study control is a person who **does not** provide unpaid care to any family members, friends, neighbours or others because of: long-term physical or mental ill-health or disability, or problems related to old age. Study controls are often recruited from GP practices.

To join this study is voluntary. You may refuse to join, or you may withdraw your consent to be in the study, for any reason. By reading this information and signing the consent form (attached to this document) you are indicating your willingness to participate in this study. Once you have signed the consent form you will be asked to complete an eligibility screening questionnaire to gather information about your past medical history and any existing care giving commitments that you have to family members, friends, neighbours or others because of long-term physical or mental ill health or disability, or problems related to old age. After you have completed these questions, the investigators can decide if you are a candidate for this study and you will be contacted by telephone or in person and given further instructions at that point.

Research studies are designed to obtain new knowledge that may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies.

Deciding not to be in the study or leaving the study before it is finished will not affect your relationship with your general practitioner, the researcher, your health care provider or the University of Glasgow.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study. You should ask the researchers named above any questions that you have about this study at any time.

Why are we doing this study?

One in ten of the UK population provides help and support to family members, friends, neighbours or others because of: long-term physical or mental health ill health or disability, or problems related to old age. This informal caring network provides a huge benefit to society by preventing

people going into costly care homes. Stroke is a major cause of adult disability and at any one time 0.5% of the UK population are dependent as the result of a stroke. Much of the burden of providing for the needs of these people falls to the informal carer often a family member or close friend. Providing help and support to a stroke survivor can be hard, and can sometimes lead to stress.

We would like to follow-up a group of people who look after, help or provide support to stroke survivors. We would also like to follow-up a similar group of people who do not provide look after, or give help or support to any family members, friends, neighbours or others because of: long-term physical or mental ill-health or disability, or problems related to old age. To help us to find this out, we need to have a similar group of people who do not provide care to compare the carers to.

The purpose of doing this study is to assess the effects of looking after, helping or providing support to stroke survivors on the health of the person who is providing the care.

Who should participate?

- Are you aged over sixteen?

If you are aged over 16, please read on before making you decision to participate in the study.

What will happen during the study?

First, a research nurse will review the study protocol and potential risks and benefits of the study with you. Then, you will be asked to complete a series of more in-depth questionnaires, at the point where you join the study, at three months and six months. These questionnaires will ask you

a series of questions relating to your health and well-being and the help you get from friends and family.

When will I do this?

You will be asked to complete a questionnaire when you enter the study, then three months and six months later.

How long will it take me?

Each questionnaire will take on average 25 minutes to complete.

What will happen?

We hope to be able to work closely with each person who has agreed to take part in the study. We will arrange with you the most suitable and convenient way for you to complete the questionnaires. This may be in person with the study researcher, by telephone or by post.

If you choose to complete the questionnaires with the study researcher you can choose a venue and a time which is most convenient for you, for example at home, or at a stroke clinic. If you choose to complete the questionnaire by telephone we will again arrange a time that suits you. If you choose to return the questionnaires by post we will provide you with a stamped addressed envelope.

We understand that everyone has very busy lives therefore our aim is to make participation in this study as simple, quick and convenient as possible.

How many people will take part in this study?

We are hoping to recruit 115 carers and 115 non-care giving people.

How will your privacy be protected?

The information contained in each of the questionnaires will be entered into a computer package, which will allow the data to be analysed. At all times electronic data (that is, information stored electronically on computer drives and disks) will remain in password-protected computer files. Paper copies, including completed questionnaires, will be stored in locked filing cabinets. Carer contact information and survey data will be stored in separate locations and/or computer files whenever possible. To further protect the identity of the study participants, each person participating in a study will be assigned a subject number, which will be used whenever possible instead of that person's name.

Identifiable study data will only be transported between sites (for example, from the Stroke Services, Stobhill Hospital to the Academic Section of Geriatric Medicine, Glasgow Royal Infirmary, University of Glasgow) using email with highly secure encryption technology.

Will there be potential harm during the study?

While we have made every attempt to make the questionnaires as unobtrusive as possible we realize that some of the questions may be quite personal in nature. If you feel at all uncomfortable answering any of the questions, you are free to skip a question and move to the next one.

Once you have completed a questionnaire, you might feel like you would like to talk to someone. If this does happen, then the researcher will discuss with you the available options.

Will information from the study be given to my GP?

We will write a letter to your GP to tell them that you are involved in this study.

What are the benefits if I participate in the study?

There may be no direct benefits to you personally for participating in this study. However, the information will help us to understand the impact of providing care to stroke survivors. It will also enable us to develop ways of identifying carers who would benefit from extra help and also to find out what kind of specific services, activities or products should be developed in the future.

Who will know what I said in the questionnaires?

A member of the Glasgow Cohort Study research team will administer and collect the questionnaires. Lynn Legg, the study's principal investigator will enter the questionnaire responses onto a computer package. Lynn Legg and Professor Peter Langhorne, the principal investigators, will analyse the data, however, your name will not be attached to the data being analysed. The findings will be included in a report to the Chief Scientist Office, Scotland and will also form the basis of a PhD thesis. We also expect that the study results will be published in stroke specific and general medical journals as well as presented at national and international conferences. Again, personal information or other identifying information will not be included in any reports. Your personal information collected in this form is for this research project only. This information will be kept in confidence. This information will not be used for any other purpose or disclosed without your consent.

What if I change my mind about participating in the study?

Your participation is voluntary. You may decide to withdraw from the study at any time with no further consequence to you. Your decision will not affect the health care that is provided to the person that you care for or increase their length of stay in hospital.

Will I have access to the final report?

The written report of the study will be available to you if you wish.

Who do I contact to participate or for more information?

If you have questions about this project, please call:

Lynn Legg on 0141 211 4953

**APPENDIX 9: THE GLASGOW CARERS COHORT STUDY
UNEXPOSED PARTICIPANT CONSENT FORM**

Telephone: 0141 211 4976

Date:

Academic Section of Geriatric Medicine
3rd Floor University Block
Royal Infirmary
Alexandra Parade
Glasgow, G31 2ER

Centre Number:



CONTROL CONSENT FORM

Title: The Glasgow Carers Cohort Study

Name of Researchers: Lynn Legg and Peter Langhorne
Academic Section of Geriatric Medicine, 3rd floor University Block, Royal
Infirmary, Glasgow, G31 2ER. Telephone: 0141 211 4953

Please initial box

4. I confirm that I have read and understand the information sheet for the above study and have had the opportunity to ask questions.

5. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

6. I agree to continue to take part in the above study.

_____	_____	_____
Name of Carer	Date	Signature
_____	_____	_____
Name of Person taking consent (if different from researcher)	Date	Signature
_____	_____	_____
Researcher	Date	Signature

**APPENDIX 10: THE GLASGOW CARERS COHORT STUDY
UNEXPOSED PARTICIPANT SCREENING FORM**

1. Do you look after, or give help or support to any other family members, friends, neighbours or others because of: long-term physical or mental ill-health or disability, or problems related to old age?

- No
- Yes, 1-19 hours a week
- Yes, 20-49 hours a week
- Yes, 50+ hours a week

CHRONIC HEALTH CONDITIONS

We are interested in any chronic health conditions that you may have. We are interested in ‘long-term conditions’ that have or are expected to last more than 6 months and that have been diagnosed by a doctor.

1. Has your doctor ever told you that you have:
 ✓ All boxes that apply

- *Cirrhosis or liver disease
- *Diabetes
- *Eye, kidney or nerve damage due to diabetes
- *Heart failure
- *Heart attack
- *Stroke
- *Hardening of the arteries/poor circulation
- *Ulcer (peptic, stomach, duodenal)
- *Hemiplegia
- *Cancer
- *Any malignant tumour
- *Leukaemia
- *Lymphoma
- *Chronic asthma
- *Chronic bronchitis
- *Chronic obstructive pulmonary disease
- *Emphysema
- *Fibrosis
- *Pneumoconiosis
- *Dementia

- *All other arthritis e.g. rheumatoid arthritis, systemic lupus erythematosus, scleroderma etc
- *Kidney problems.
- *Severe kidney disease (dialysis, transplant).

SECTION 7: MEDICATIONS

The next set of questions are about use of medications, both prescription and over-the-counter, as well as other health products.

1. In the past month, have you taken any medications prescribed by your doctor?

- Yes
- No

2. Can you please list the medications (that the doctor has prescribed for you) that you have taken over the last month?

Drug e.g. aspirin,

There are many other health products such as ointments, vitamins, herbs, minerals or protein drinks which people use to prevent illness or to improve or maintain their health.

2. In the past month, have you used any ointments, vitamins, herbs, minerals or protein drinks?

Yes

No

Can you please list the ointments, vitamins, herbs, minerals or protein drinks that you have taken over the last month?

Drug e.g. St. John's Wort, Vitamin C

Thank you!

**APPENDIX 11: THE GLASGOW CARERS COHORT STUDY
UNEXPOSED PARTICIPANT BASELINE QUESTIONNAIRE**



University
of Glasgow



SECTION 1: NAME AND ADDRESS

1. What is your name?
2. What is your address?
3. Post code?
4. What is your telephone number? (In case we need to contact you)
5. What is your mobile telephone number (In case we need to contact you)

SECTION 2 GENERAL PRACTITIONER (GP) DETAILS

1. What is your GPs name?
2. What is your GPs address?
3. What is your GPs telephone number?

SECTION 3: ABOUT YOU

1. What is your sex? (Please circle one)

Male Female

2. What is your date of birth?

--	--	--	--	--	--	--	--

3. What is your marital status? (Please tick)

Single
 Married
 Separated or divorced
 Widowed

ETHNIC GROUP

5. What is your ethnic group? (Please circle)

1. White

Scottish
 Other British
 Irish
 Other white background

2. Mixed

Any mixed background

3. Asian, Asian Scottish or Asian British

Indian
 Pakistani
 Bangladeshi
 Chinese
 Other Asian background

4. Black, Black Scottish or Black

British
 Caribbean

African
Other black background

5. Other ethnic background

EMPLOYMENT

If you are aged 16-74 please complete go to Question 6.

If you are age 75 and over please go to Question 8.

Last week were you doing any work:

as an employee?
as self-employed/ freelance?
in your own family business? or
on a government training scheme?

'Yes', if you were away from work ill, on maternity leave, on holiday or temporarily laid off.

'Yes' for any paid work including casual or temporary work, even if only for one hour.

'Yes', if you worked paid or unpaid, in your own / family business

'Yes', go to question 8

'No', go to question 7

7. Last week were you any of the following? (Please circle)

Retired
Student
Looking after home/ family
Permanently sick/ disabled
None of the above

Go to question 9 'Qualifications'.

8. How many hours (to the nearest full hour) a week do you usually work in your main job?

Give average for last 4 weeks
Number of hours worked a wee

QUALIFICATIONS

9. Which of these qualifications do you have?

✓ All boxes that apply

- 'O'Grade, Standard Grade, Intermediate 1, Intermediate 2, GCSE, CSE, Senior Certificate or equivalent
- Higher Grade, CSYS, Scottish Group Award at higher, 'A' Level, AS Level, Advanced Senior Certificate or equivalent
- GSVQ/SVQ Level 1 or 2, SCOTVEC/National Certificate Module, BTEC First Diploma, City and Guilds Craft, RSA Diploma or equivalent
- GSVQ/SVQ Level 3, ONC, OND, SCOTVEC National Diploma, City and Guilds Advanced Craft, RSA Advanced Diploma or equivalent
- First Degree, Higher Degree
- Professional Qualifications (for example teaching, accountancy)
- None of these

SECTION 4: ABOUT YOUR GENERAL HEALTH

1. In general, would you say that your health is: (please circle one)

Excellent
 Very good
 Good
 Fair
 Poor

2. Compared to one year ago, how would you rate your general health now?
 (Circle one number)

- 1 Much better than one year ago
- 2 Somewhat better than one year ago
- 3 About the same as one year ago
- 4 Somewhat worse than one year ago
- 5 Much worse than one year ago

The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? (Circle one number)

3. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports.

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

4. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf.

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

5. Lifting or carrying groceries.

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

6. Climbing several flights of stairs

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

7. Climbing one flight of stairs

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

8. Bending, kneeling, or stooping

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

9. Walking more than a mile

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

10. Walking several hundred yards

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

11. Walking one hundred yards

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

12. Bathing or dressing yourself

- 1 Yes, limited a lot
- 2 Yes, limited a little
- 3 No, not limited at all

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

(Circle yes or no)

13. Cut down the amount of time you spent on work or other activities

Yes No

14. Accomplished less than you would like

Yes No

15. Were limited in the kind of work or other activities

Yes No

16. Had difficulty performing the work or other activities (for example, it took extra effort)

Yes No

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

(Circle yes or no)

17. Cut down the amount of time you spent on work or other activities

Yes No

18. Accomplished less than you would like

Yes No

19. Didn't do work or other activities as carefully as usual

Yes No

20. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups? (Circle one number)

- 1 Not at all
- 2 Slightly
- 3 Moderately
- 4 Severe
- 5 Very severe

21. How much bodily pain have you had during the past 4 weeks?

- 1 None
- 2 Very Mild
- 3 Mild
- 4 Moderate
- 5 Severe
- 6 Very severe

22. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

- 1 Not at all
- 2 A little bit
- 3 Moderately
- 4 Quite a bit
- 5 Extremely

These questions are about how you feel and how things have been with you during the last 4 weeks. For each question, please give the answer that comes closest to the way you have been feeling.

23. Did you feel full of pep?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

24. Have you been a very nervous person?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

25. Have you felt so down in the dumps that nothing could cheer you up?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

26. Have you felt calm and peaceful?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

27. Did you have a lot of energy?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

28. Have you felt downhearted and blue?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

29. Did you feel worn out?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

30. Have you been a happy person?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

31. Did you feel tired?

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

32. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

(Circle one number)

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time

- 4 Some of the time
- 5 A little bit of the time
- 6 None of the time

How true or false is each of the following statements for you?
(Circle one number)

33. I seem to get sick a little easier than other people

- 1 Definitely true
- 2 Mostly true
- 3 Don't know
- 4 Mostly false
- 5 Definitely false

34. I am as healthy as anybody I know

- 1 Definitely true
- 2 Mostly true
- 3 Don't know
- 4 Mostly false
- 5 Definitely false

35. I expect my health to get worse

- 1 Definitely true
- 2 Mostly true
- 3 Don't know
- 4 Mostly false
- 5 Definitely false

36. My health is excellent

- 1 Definitely true
- 2 Mostly true
- 3 Don't know
- 4 Mostly false
- 5 Definitely false

SECTION 5: HOW YOU FEEL

On the next page are a number of statements about your well being. Would you please indicate how much you agree or disagree by circling number beside the statement you have picked.

1. I don't feel particularly pleased with the way I am

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

2. I feel that life is very rewarding

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

3. I am well satisfied about everything in my life

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

4. I don't think I look attractive

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

5. I find beauty in some things

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

6. I can fit in everything I want to

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

7. I feel fully mentally alert

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

8. I do not have particularly happy memories of the past

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

This section consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the **one statement** in each group that best describes the way you have been feeling during the past two weeks, including today. Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (Changes in Sleeping Pattern) or Item 18. (Changes in Appetite).

1. Sadness

- 1 I do not feel sad.
- 2 I feel sad much of the time.
- 3 I am sad all the time.
- 4 I am so sad or unhappy that I can't stand it.

2. Pessimism

- 1 I am not discouraged about my future.
- 2 I feel more discouraged about my future than I used to be.
- 3 I do not expect things to work out for me.
- 4 I feel my future is hopeless and will only get worse.

3. Past Failure

- 1 I do not feel like a failure
- 2 I have failed more than I should have.
- 3 As I look back, I see a lot of failures.
- 4 I feel I am a total failure as a person

4. Loss of Pleasure

- 1 I get as much pleasure as I ever did from the things I enjoy.
- 2 I don't enjoy things as much as I used to.
- 3 I get very little pleasure from the things I used to enjoy.
- 4 I can't get any pleasure from the things I used to enjoy.

5. Guilty Feelings

- 1 I don't feel particularly guilty.
- 2 I feel guilty over many things I have done or should have done.
- 3 I feel quite guilty most of the time.
- 4 I feel guilty all of the time.

6. Punishment Feelings

- 1 I don't feel I am being punished.
- 2 I feel I may be punished.
- 3 I expect to be punished.
- 4 I feel I am being punished.

7. Self-Dislike

- 1 I feel the same about myself as ever.
- 2 I have lost confidence in myself.
- 3 I am disappointed in myself.
- 4 I dislike myself.

8. Self-Criticalness

- 1 I don't criticize or blame myself more than usual.
- 2 I am more critical of myself than I used to be.
- 3 I criticize myself for all of my faults.

4 I blame myself for everything bad that happens.

9. Suicidal Thoughts or Wishes

- 1 I don't have any thoughts of killing myself.
- 2 I have thoughts of killing myself, but I would not carry them out.
- 3 I would like to kill myself.
- 4 I would kill myself if I had the chance.

10. Crying

- 1 I don't cry anymore than I used to.
- 2 I cry more than I used to.
- 3 I cry over every little thing.
- 4 I feel like crying, but I can't.

11. Agitation

- 1 I am no more restless or wound up than usual.
- 2 I feel more restless or wound up than usual.
- 3 I am so restless or agitated that it's hard to stay still.
- 4 I am so restless or agitated that I have to keep moving or doing something.

12. Loss of Interest

- 1 I have not lost interest in other people or activities.
- 2 I am less interested in other people or things than before.
- 3 I have lost most of my interest in other people or things.
- 4 It's hard to get interested in anything.

13. Indecisiveness

- 1 I make decisions about as well as ever.
- 2 I find it more difficult to make decisions than usual.
- 3 I have much greater difficulty decisions than I used to.
- 4 I have trouble making any decisions.

14. Worthlessness

- 1 I do not feel I am worthless.
- 2 I don't consider myself as worthwhile and useful as I used to.
- 3 I feel more worthless as compared to other people.
- 4 I feel utterly worthless.

15. Loss of Energy

- 1 I have as much energy as ever.
- 2 I have less energy than I used to have.
- 3 I don't have enough energy to do very much.
- 4 I don't have enough energy to do anything.

16. Changes in Sleeping Pattern

- 0 I have not experienced any change in my sleeping pattern
- 1a I sleep somewhat more than usual.
- 1b I sleep somewhat less than usual.
- 2a I sleep a lot more than usual.
- 2b I sleep a lot less than usual.
- 3a I sleep most of the day
- 3b I wake up 1-2 hours early and cannot get back to sleep.

17. Irritability

- 1 I am no more irritable than usual.
- 2 I am more irritable than usual.
- 3 I am much more irritable than usual.
- 4 I am irritable all the time.

18. Changes in Appetite

- 0 I have not experienced any change in my appetite.
- 1a My appetite is somewhat less than usual.
- 1b My appetite is somewhat greater than usual.
- 2a My appetite is much less than before.
- 2b My appetite is much greater than usual.
- 3a I have no appetite at all.
- 3b I crave food all the time.

19. Concentration Difficulty

- 1 I can concentrate as well as ever.
- 2 I can't concentrate as well as usual.
- 3 It's hard to keep my mind on anything for very long.
- 4 I find I can't concentrate on anything.

20. Tiredness or Fatigue

- 1 I am no more tired or fatigued than usual.
- 2 I get more tired or fatigued more easily than usual.
- 3 I am too tired or fatigued to do a lot of the things I used to do.

4 I am too tired or fatigued to do most of the things I used to do.

21. Loss of Interest in Sex

- 1 I have not noticed any recent change in my interest in sex.
- 2 I am less interested in sex than I used to be.
- 3 I am much less interested in sex now.
- 4 I have lost interest in sex completely.
- 5 Not applicable

SECTION 5: HOW YOU ARE COPING

These questions about your feelings and thoughts during the last month. In each case, please circle the number that indicates how often you felt or thought a certain way.

1. In the last month, how often have you been upset because of something that happened unexpectedly?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

2. In the last month, how often have you felt that you were unable to control the important things in your life?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

3. In the last month, how often have you felt nervous and "stressed"?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

4. In the last month, how often have you felt confident about your ability to handle your personal problems?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

5. In the last month, how often have you felt that things were going your way?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

6. In the last month, how often have you found that you could not cope with all the things that you had to do?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

7. In the last month, how often have you been able to control irritations in your life?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

8. In the last month, how often have you felt that you were on top of things?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

9. In the last month, how often have you been angered because of things that were outside of your control?

- 1 Never
- 2 Almost never

- 3 Sometimes
- 4 Fairly often
- 5 Very often

10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

SECTION 5: SYMPTOMS

During the past month, how much have you been bothered by any of the following problems?

1. Stomach problems

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

2. Back pain

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

3. Pain in your arms, legs, or joints (knees, hips, etc)

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

4. Menstrual cramps or other problems with your periods (women only)

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

5. Headaches

- 1 Not bothered at all

- 2 Bothered a little
- 3 Bothered a lot

6. Chest pain

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

7. Dizziness

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

8. Fainting spells

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

9. Feeling your heart pound or race

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

10. Shortness of breath

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

11. Pain or problems during sexual intercourse

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

12. Constipation, loose bowels or diarrhea

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

13. Nausea, gas, or indigestion

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

14. Feeling tired or having low energy

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

15. Trouble sleeping

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

SECTION 6: HISTORY OF DEPRESSION

The next set of questions asks about your personal medical history of depression.

1. Have you ever had one or several episodes of being sad, depressed, discouraged or uninterested most of the day, for several days, weeks and longer?
(Please circle one)

- Yes
- No
- Don't know

2. Have you ever been diagnosed with depression by a health professional?
(Please circle one)

- Yes
- No
- Don't know

SECTION 7: MEDICATIONS

The next set of questions are about use of medications, both prescription and over-the-counter, as well as other health products.

1. In the past month, have you taken any medications prescribed by your doctor?

Yes

No

Can you please list the medications (that the doctor has prescribed for you) that you have taken over the last month?

<p>Drug e.g. aspirin,</p>

Over the counter medications

<p>There are many other health products such as ointments, vitamins, herbs, minerals or protein drinks which people use to prevent illness or to improve or maintain their health.</p>
--

2. In the past month, have you used any ointments, vitamins, herbs, minerals or protein drinks? (Please circle yes or no)

Yes
No

Can you please list the ointments, vitamins, herbs, minerals or protein drinks that you have taken over the last month?

<p>Drug e.g. St. John's Wort, Vitamin C</p>

SECTION 8: SMOKING

1. Have you ever smoked cigarettes at all? (Please circle yes or no)

Yes
No

2. At the present time do you smoke cigarettes daily, occasionally or not at all?
(Circle one number)

Daily
Occasionally
Not at all

3. How many cigarettes do you smoke each day now?

None
1-14 cigarettes/day?
15-24 cigarettes/ day?
≥25 cigarettes/day

SECTION 9: ALCOHOL

1. How often do you have a drink containing alcohol for example beer, wine, spirits or any other alcoholic drink? (Circle one number)

Never
Monthly or less
Two to four time a week
Four or more times a week

2. How many drinks containing **alcohol** do you have on a typical day when you are drinking?

1 or 2
3 or 4
5 or 6
7 or 9

1 drink = ½ pint beer or 1 measure of spirit or one glass of wine

SECTION 10: OTHER WORRIES

1. Are you worried about any financial debt that you might be in?

Yes
No

Would you mind having one last check to make sure that you have answered all the questions?

**APPENDIX 12: THE GLASGOW CARERS COHORT EXPOSED
PARTICIPANT THREE MONTH QUESTIONNAIRES**



The Glasgow Carer's
Cohort Study



University
of Glasgow



SECTION 1: NAME AND ADDRESS

1. What is your name?
2. What is your address?
3. Post code?
4. What is your telephone number? (In case we need to contact you)
5. What is your mobile telephone number (In case we need to contact you)

SECTION 2 GENERAL PRACTITIONER (GP) DETAILS

1. What is your GPs name?
2. What is your GPs address?
3. What is your GPs telephone number?

SECTION 3: THE HELP YOU PROVIDE

Activities of daily living are the things we do during a typical day this includes any daily activity we perform for self-care (such as feeding ourselves, bathing, dressing, grooming), work, homemaking, and leisure."

The following questions are about activities you might help the person that you care for do during a typical day.

Which of the following activities do you provide regular help with?

1. Bathing

Yes No

2. Dressing and undressing

Yes No

3. Eating

Yes No

4. Transferring from bed to chair, and back

Yes No

5. Control urinary and faecal discharge (e.g. using catheters)

Yes No

6. Using the toilet

Yes No

7. Walk from one place to another

Yes No

8. Light housework

Yes No

9. Preparing meals

Yes No

10. Taking medications

Yes No

11. Shopping for groceries or clothes

Yes No

12. Using the telephone

Yes No

13. Managing money

Yes No

14. Keeping him or her company

Yes No

15. Keeping him or her safe

Yes No

16. Providing emotional support

Yes No

17. Other, please specify:

Yes No

18. How many hours per week do you give help or support to the person that you care for? Please circle.

None, I don't provide any help or support

1-19 hours a week

20-49 hours a week

50+ hours a week

SECTION 4: HOW PROVIDING HELP OR SUPPORT AFFECTS YOU

Below is a list of things that other people have found to be difficult. In each case, please circle 'yes' if they apply to you and 'no' if they don't.

1. My sleep is disturbed (For example: the person I care for is in and out of bed or wanders around at night)

Yes No

2. Caregiving is inconvenient (For example: helping takes so much time or it's a long drive over to help)

Yes No

3. Caregiving is a physical strain (For example: lifting in or out of a chair; effort or concentration is required)

Yes No

4. Caregiving is confining (For example: helping restricts free time or I cannot go visiting)

Yes No

5. There have been family adjustments (For example: helping has disrupted my routine; there is no privacy)

Yes No

6. There have been changes in personal plans (For example: I had to turn down a job; I could not go on vacation)

Yes No

7. There have been other demands on my time (For example: other family members need me)

Yes No

8. There have been emotional adjustments (For example: severe arguments about caregiving)

Yes No

9. Some behaviour is upsetting (For example: incontinence; the person cared for has trouble remembering things; or the person I care for accuses people of taking things)

Yes No

10. It is upsetting to find the person I care for has changed so much from his/her former self (For example: he/she is a different person than he/she used to be)

Yes No

11. There have been work adjustments (For example: I have to take time off for caregiving duties)

Yes No

12. Care giving is a financial strain

Yes No

13. I feel completely overwhelmed (For example: I worry about the person I care for; I have concern)

Yes No

SECTION 5: HOW YOU FEEL

On the next page are a number of statements about your well being. Would you please indicate how much you agree or disagree by circling number beside the statement you have picked.

1. I don't feel particularly pleased with the way I am

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

2. I feel that life is very rewarding

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

3. I am well satisfied about everything in my life

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

4. I don't think I look attractive

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

5. I find beauty in some things

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- 4 Slightly agree
- 5 Moderately agree
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6. I can fit in everything I want to

- 1 Strongly disagree
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- 4 Slightly agree
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7. I feel fully mentally alert

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

8. I do not have particularly happy memories of the past

- 1 Strongly disagree
- 2 Moderately disagree
- 3 Slightly disagree
- 4 Slightly agree
- 5 Moderately agree
- 6 Strongly agree

This section consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the **one statement** in each group that best describes the way you have been feeling during the past two weeks, including today. Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (Changes in Sleeping Pattern) or Item 18. (Changes in Appetite).

1. Sadness

- 1 I do not feel sad.
- 2 I feel sad much of the time.
- 3 I am sad all the time.
- 4 I am so sad or unhappy that I can't stand it.

2. Pessimism

- 1 I am not discouraged about my future.
- 2 I feel more discouraged about my future than I used to be.
- 3 I do not expect things to work out for me.
- 4 I feel my future is hopeless and will only get worse.

3. Past Failure

- 1 I do not feel like a failure.
- 2 I have failed more than I should have.
- 3 As I look back, I see a lot of failures.
- 4 I feel I am a total failure as a person.

4. Loss of Pleasure

- 1 I get as much pleasure as I ever did from the things I enjoy.
- 2 I don't enjoy things as much as I used to.
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- 4 I can't get any pleasure from the things I used to enjoy.

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- 1 I don't feel particularly guilty.
- 2 I feel guilty over many things I have done or should have done.
- 3 I feel quite guilty most of the time.
- 4 I feel guilty all of the time.

6. Punishment Feelings

- 1 I don't feel I am being punished.
- 2 I feel I may be punished.
- 3 I expect to be punished.
- 4 I feel I am being punished.

7. Self-Dislike

- 1 I feel the same about myself as ever.
- 2 I have lost confidence in myself.
- 3 I am disappointed in myself.
- 4 I dislike myself.

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- 1 I don't criticize or blame myself more than usual.
- 2 I am more critical of myself than I used to be.
- 3 I criticize myself for all of my faults.
- 4 I blame myself for everything bad that happens.

9. Suicidal Thoughts or Wishes

- 1 I don't have any thoughts of killing myself.
- 2 I have thoughts of killing myself, but I would not carry them out.
- 3 I would like to kill myself.
- 4 I would kill myself if I had the chance.

10. Crying

- 1 I don't cry anymore than I used to.
- 2 I cry more than I used to.
- 3 I cry over every little thing.
- 4 I feel like crying, but I can't.

11. Agitation

- 1 I am no more restless or wound up than usual.

- 2 I feel more restless or wound up than usual.
- 3 I am so restless or agitated that it's hard to stay still.
- 4 I am so restless or agitated that I have to keep moving or doing something.

12. Loss of Interest

- 1 I have not lost interest in other people or activities.
- 2 I am less interested in other people or things than before.
- 3 I have lost most of my interest in other people or things.
- 4 It's hard to get interested in anything.

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14. Worthlessness

- 1 I do not feel I am worthless.
- 2 I don't consider myself as worthwhile and useful as I used to.
- 3 I feel more worthless as compared to other people.
- 4 I feel utterly worthless.

15. Loss of Energy

- 1 I have as much energy as ever.
- 2 I have less energy than I used to have.
- 3 I don't have enough energy to do very much.
- 4 I don't have enough energy to do anything.

16. Changes in Sleeping Pattern

- 0 I have not experienced any change in my sleeping pattern
- 1a I sleep somewhat more than usual.
- 1b I sleep somewhat less than usual.
- 2a I sleep a lot more than usual.
- 2b I sleep a lot less than usual.
- 3a I sleep most of the day
- 3b I wake up 1-2 hours early and cannot get back to sleep.

17. Irritability

- 1 I am no more irritable than usual.

- 2 I am more irritable than usual.
- 3 I am much more irritable than usual.
- 4 I am irritable all the time.

18. Changes in Appetite

- 0 I have not experienced any change in my appetite.
- 1a My appetite is somewhat less than usual.
- 1b My appetite is somewhat greater than usual.
- 2a My appetite is much less than before.
- 2b My appetite is much greater than usual.
- 3a I have no appetite at all.
- 3b I crave food all the time.

19. Concentration Difficulty

- 1 I can concentrate as well as ever.
- 2 I can't concentrate as well as usual.
- 3 It's hard to keep my mind on anything for very long.
- 4 I find I can't concentrate on anything.

20. Tiredness or Fatigue

- 1 I am no more tired or fatigued than usual.
- 2 I get more tired or fatigued more easily than usual.
- 3 I am too tired or fatigued to do a lot of the things I used to do.
- 4 I am too tired or fatigued to do most of the things I used to do.

21. Loss of Interest in Sex

- 1 I have not noticed any recent change in my interest in sex.
- 2 I am less interested in sex than I used to be.
- 3 I am much less interested in sex now.
- 4 I have lost interest in sex completely.
- 5 Not applicable

SECTION 5: HOW YOU ARE COPING

These questions about your feelings and thoughts during the last month. In each case, please circle the number that indicates how often you felt or thought a certain way.

- 1. In the last month, how often have you been upset because of something that happened unexpectedly?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

2. In the last month, how often have you felt that you were unable to control the important things in your life?

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3. In the last month, how often have you felt nervous and "stressed"?

- 1 Never
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4. In the last month, how often have you felt confident about your ability to handle your personal problems?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

5. In the last month, how often have you felt that things were going your way?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

6. In the last month, how often have you found that you could not cope with all the things that you had to do?

- 1 Never
- 2 Almost never

- 3 Sometimes
- 4 Fairly often
- 5 Very often

7. In the last month, how often have you been able to control irritations in your life?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

8. In the last month, how often have you felt that you were on top of things?

- 1 Never
- 2 Almost never
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- 4 Fairly often
- 5 Very often

9. In the last month, how often have you been angered because of things that were outside of your control?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?

- 1 Never
- 2 Almost never
- 3 Sometimes
- 4 Fairly often
- 5 Very often

SECTION 5: SYMPTOMS

During the past month, how much have you been bothered by any of the following problems?

- 1. Stomach problems

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

2. Back pain

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

3. Pain in your arms, legs, or joints (knees, hips, etc)

- 1 Not bothered at all
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- 3 Bothered a lot

4. Menstrual cramps or other problems with your periods (women only)

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

5. Headaches

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

6. Chest pain

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

7. Dizziness

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

8. Fainting spells

- 1 Not bothered at all
- 2 Bothered a little

3 Bothered a lot

9. Feeling your heart pound or race

1 Not bothered at all

2 Bothered a little

3 Bothered a lot

10. Shortness of breath

1 Not bothered at all

2 Bothered a little

3 Bothered a lot

11. Pain or problems during sexual intercourse

1 Not bothered at all

2 Bothered a little

3 Bothered a lot

12. Constipation, loose bowels or diarrhea

1 Not bothered at all

2 Bothered a little

3 Bothered a lot

13. Nausea, gas, or indigestion

1 Not bothered at all

2 Bothered a little

3 Bothered a lot

14. Feeling tired or having low energy

1 Not bothered at all

2 Bothered a little

3 Bothered a lot

15. Trouble sleeping

1 Not bothered at all

2 Bothered a little

3 Bothered a lot

SECTION 6: SOCIAL SUPPORT

People sometimes look to others for companionship, assistance, or other types of support. This section covers the types of support that would be available to you if you needed it. Please check the most appropriate response based on the support available to you in the last four weeks.

How often is someone available...

1.... to take you to the doctor if you need to go?

- 1 None of the time
- 2 A little of the time
- 3 Some of the time
- 4 Most of the time
- 5 All of the time

2. ... someone to have a good time with?

- 1 None of the time
- 2 A little of the time
- 3 Some of the time
- 4 Most of the time
- 5 All of the time

3. ... to hug you?

- 1 None of the time
- 2 A little of the time
- 3 Some of the time
- 4 Most of the time
- 5 All of the time

4. ... to prepare your meals if you were unable to do it yourself?

- 1 None of the time
- 2 A little of the time
- 3 Some of the time
- 4 Most of the time
- 5 All of the time

5. ...to understand your problems?

- 1 None of the time
- 2 A little of the time
- 3 Some of the time
- 4 Most of the time
- 5 All of the time

SECTION 7: MEDICATIONS

The next set of questions are about use of medications, both prescription and over-the-counter, as well as other health products.

1. In the past month, have you taken any medications prescribed by your doctor?

Yes
No

Can you please list the medications (that the doctor has prescribed for you) that you have taken over the last month?

Drug e.g. aspirin,

Over the counter medications

There are many other health products such as ointments, vitamins, herbs, minerals or protein drinks which people use to prevent illness or to improve or maintain their health.

2. In the past month, have you used any ointments, vitamins, herbs, minerals or protein drinks? (Please circle yes or no)

Yes
No

Can you please list the ointments, vitamins, herbs, minerals or protein drinks that you have taken over the last month?

Drug e.g. St. John's Wort, Vitamin C

SECTION 8: SMOKING

1. Have you ever smoked cigarettes at all? (Please circle yes or no)

Yes

No

2. At the present time do you smoke cigarettes daily, occasionally or not at all?
(Circle one number)

1 Daily

2 Occasionally

3 Not at all

3. How many cigarettes do you smoke each day now?

None

1-14 cigarettes/day?

15-24 cigarettes/day?

≥25 cigarettes/day

SECTION 9: ALCOHOL

1. How often do you have a drink containing alcohol for example beer, wine, spirits or any other alcoholic drink? (Circle one number)

Never

Monthly or less

Two to four time a week

Four or more times a week

2. How many drinks containing **alcohol** do you have on a typical day when you are drinking?

1 or 2

3 or 4

5 or 6
7 or 9

1 drink = ½ pint beer or 1 measure of spirit or one glass of wine

SECTION 10: OTHER WORRIES

1. Are you worried about any financial debt that you might be in?

Yes
No

Would you mind having one last check to make sure that you have answered all the questions?

**APPENDIX 13: THE GLASGOW CARERS COHORT UNEXPOSED
PARTICIPANT THREE MONTH QUESTIONNAIRE**



The Glasgow Carer's
Cohort Study



University
of Glasgow



SECTION 1: NAME AND ADDRESS

1. What is your name?
2. What is your address?
3. Post code?
4. What is your telephone number? (In case we need to contact you)
5. What is your mobile telephone number (In case we need to contact you)

SECTION 2 GENERAL PRACTITIONER (GP) DETAILS

1. What is your GPs name?
2. What is your GPs address?
3. What is your GPs telephone number?

SECTION 3: THE HELP YOU PROVIDE

Not to be completed

SECTION 4: HOW PROVIDING HELP OR SUPPORT AFFECTS YOU

Not to be completed

SECTION 5: HOW YOU FEEL

On the next page are a number of statements about your well being. Would you please indicate how much you agree or disagree by circling number beside the statement you have picked.

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- 1 Strongly disagree
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4. I don't think I look attractive

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5. I find beauty in some things

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- 3 I feel more worthless as compared to other people.
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15. Loss of Energy

- 1 I have as much energy as ever.
- 2 I have less energy than I used to have.
- 3 I don't have enough energy to do very much.
- 4 I don't have enough energy to do anything.

16. Changes in Sleeping Pattern

- 0 I have not experienced any change in my sleeping pattern
- 1a I sleep somewhat more than usual.
- 1b I sleep somewhat less than usual.
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- 2b I sleep a lot less than usual.
- 3a I sleep most of the day
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17. Irritability

- 1 I am no more irritable than usual.
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- 3b I crave food all the time.

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- 1 I can concentrate as well as ever.
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21. Loss of Interest in Sex

- 1 I have not noticed any recent change in my interest in sex.
- 2 I am less interested in sex than I used to be.
- 3 I am much less interested in sex now.
- 4 I have lost interest in sex completely.
- 5 Not applicable

SECTION 5: HOW YOU ARE COPING

These questions about your feelings and thoughts during the last month. In each case, please circle the number that indicates how often you felt or thought a certain way.

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11. Pain or problems during sexual intercourse

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12. Constipation, loose bowels or diarrhea

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13. Nausea, gas, or indigestion

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14. Feeling tired or having low energy

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

15. Trouble sleeping

- 1 Not bothered at all
- 2 Bothered a little
- 3 Bothered a lot

SECTION 6: SOCIAL SUPPORT

People sometimes look to others for companionship, assistance, or other types of support. This section covers the types of support that would be available to you if you needed it. Please check the most appropriate response based on the support available to you in the last four weeks.

How often is someone available...

1.... to take you to the doctor if you need to go?

- 1 None of the time
- 2 A little of the time

- 3 Some of the time
- 4 Most of the time
- 5 All of the time

2. ... someone to have a good time with?

- 1 None of the time
- 2 A little of the time
- 3 Some of the time
- 4 Most of the time
- 5 All of the time

3. ... to hug you?

- 1 None of the time
- 2 A little of the time
- 3 Some of the time
- 4 Most of the time
- 5 All of the time

4. ... to prepare your meals if you were unable to do it yourself?

- 1 None of the time
- 2 A little of the time
- 3 Some of the time
- 4 Most of the time
- 5 All of the time

5. ...to understand your problems?

- 1 None of the time
- 2 A little of the time
- 3 Some of the time
- 4 Most of the time
- 5 All of the time

SECTION 7: MEDICATIONS

The next set of questions are about use of medications, both prescription and over-the-counter, as well as other health products.

1. In the past month, have you taken any medications prescribed by your doctor?

Yes

No

Can you please list the medications (that the doctor has prescribed for you) that you have taken over the last month?

<p>Drug e.g. aspirin,</p>

Over the counter medications

<p>There are many other health products such as ointments, vitamins, herbs, minerals or protein drinks which people use to prevent illness or to improve or maintain their health.</p>
--

2. In the past month, have you used any ointments, vitamins, herbs, minerals or protein drinks? (Please circle yes or no)

Yes
No

Can you please list the ointments, vitamins, herbs, minerals or protein drinks that you have taken over the last month?

<p>Drug e.g. St. John's Wort, Vitamin C</p>

SECTION 8: SMOKING

1. Have you ever smoked cigarettes at all? (Please circle yes or no)

Yes
No

2. At the present time do you smoke cigarettes daily, occasionally or not at all?
(Circle one number)

- 6 Daily
- 7 Occasionally
- 8 Not at all

3. How many cigarettes do you smoke each day now?

- None
- 1-14 cigarettes/day?
- 15-24 cigarettes/ day?
- ≥25 cigarettes/day

SECTION 9: ALCOHOL

1. How often do you have a drink containing alcohol for example beer, wine, spirits or any other alcoholic drink? (Circle one number)

- Never
- Monthly or less
- Two to four time a week
- Four or more times a week

2. How many drinks containing **alcohol** do you have on a typical day when you are drinking?

- 1 or 2
- 3 or 4
- 5 or 6
- 7 or 9

1 drink = ½ pint beer or 1 measure of spirit or one glass of wine

SECTION 10: OTHER WORRIES

1. Are you worried about any financial debt that you might be in?

- Yes
- No

Would you mind having one last check to make sure that you have answered all the questions?

**APPENDIX 14: SEARCH STRATEGIES FOR CHAPTER 4 -
INCIDENCE, PREVALENCE AND ASSOCIATION BETWEEN
PROVIDING INFORMAL CARE-GIVING TO STROKE SURVIVORS AND
DEPRESSION: A SYSTEMATIC REVIEW AND META-ANALYSIS**

MEDLINE search strategy

1. carers/ or friends/ or exp parents/ or spouses/ or visitors to patients/
2. family/ or exp family characteristics/ or family relations/ or intergenerational relations/
3. family therapy/ or family nursing/ or family health.mp.
4. (carer\$ or carer\$ or care giver\$ or care-giver\$).tw.
5. (family or families or spous\$ or parent or parents or father\$ or mother\$ or friend or friends or husband\$ or wife or wives or partner or partners).tw.
6. ((home or communit\$) adj5 care).tw.
7. (home-based or community-based).tw.
8. home nursing.tw.
9. ((non-professional or non professional or informal) adj5 (care or nursing)).tw.
10. (next of kin or relatives).tw.
11. or/1-10
12. cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or cerebrovascular accident/ or exp brain infarction/ or exp hypoxia-ischemia, brain/ or exp intracranial arterial diseases/ or intracranial arteriovenous malformations/ or exp "intracranial embolism and thrombosis"/ or exp intracranial hemorrhages/ or vasospasm, intracranial/ or vertebral artery dissection/
13. (stroke or poststroke or post-stroke or cerebrovasc\$ or brain vasc\$ or cerebral vasc\$ or cva\$ or apoplex\$ or SAH).tw.
14. ((brain\$ or cerebr\$ or cerebell\$ or intracran\$ or intracerebral) adj5 (isch?emi\$ or infarct\$ or thrombo\$ or emboli\$ or occlus\$)).tw.
15. ((brain\$ or cerebr\$ or cerebell\$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage\$ or hemorrhage\$ or haematoma\$ or hematoma\$ or bleed\$)).tw.
16. hemiplegia/ or exp paresis/
17. (hemipleg\$ or hemipar\$ or paresis or paretic).tw.
18. or/12-17
19. exp DEPRESSION/
20. exp Depressive Disorder/
21. exp Dysthymic Disorder/
22. or/19-21
23. 22 and 11 and 18
24. exp cross sectional studies/
25. cross sectional.tw.
26. prospective.tw.
27. retrospective.tw.
28. exp cohort studies/
29. exp case control studies/
30. or/24-29
31. 23 and 30

32. control\$.tw.
33. 23 and 32
34. 31 or 33
35. limit 34 to human

EMBASE search strategy

1. exp cross sectional studies/
2. cross sectional.tw.
3. prospective.tw.
4. retrospective.tw.
5. exp cohort studies/
6. exp case control studies/
7. 1 or 2 or 3 or 4 or 5 or 6
8. exp cerebrovascular accident/
9. exp STROKE/
10. exp brain ischemia/
11. 8 or 9 or 10
12. 7 and 11
13. exp CARER/
14. exp home care/
15. 13 or 14
16. exp depression/
17. exp dysthymia/
18. 16 or 17
19. 12 and 15 and 18

CINHAL search strategy

- S23 S20 or S21 or S22
 S22 dysthymia
 S21 depressive disorder
 S20 depression
 S19 S7 and S13 and S18
 S18 S15 or S16 or S17
 S17 (MH "Carer Home Care Readiness (Iowa NOC)")
 S16 (MH "Age Specific Care")
 S15 (MM "Carers")
 S14 S7 and S13
 S13 S9 or S10 or S11 or S12 or S13
 S12 "cerebrovascular event"
 S11 "cerebrovascular accident"
 S10 "cerebrovascular disorder"

- S9 "stroke" OR stroke/exp OR MH stroke
- S8 "cerebrovascular attack"
- S7 S1 or S2 or S3 or S4 or S5 or S6
- S6 case control studies
- S5 cohort studies
- S4 retrospective
- S3 prospective
- S2 cross sectional
- S1 cross sectional studies

**APPENDIX 15 SEARCH STRATEGIES FOR CHAPTER 5 - NON
PHARMACOLOGICAL INTERVENTIONS FOR INFORMAL CARERS OF
STROKE SURVIVORS**

MEDLINE search strategy

1. cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or cerebrovascular accident/ or exp brain infarction/ or exp hypoxia-ischemia, brain/ or exp intracranial arterial diseases/ or intracranial arteriovenous malformations/ or exp "intracranial embolism and thrombosis"/ or exp intracranial hemorrhages/ or vasospasm, intracranial/ or vertebral artery dissection/
2. (stroke or poststroke or post-stroke or cerebrovasc\$ or brain vasc\$ or cerebral vasc\$ or cva\$ or apoplex\$ or SAH).tw.
3. ((brain\$ or cerebr\$ or cerebell\$ or intracran\$ or intracerebral) adj5 (isch?emi\$ or infarct\$ or thrombo\$ or emboli\$ or occlus\$)).tw.
4. ((brain\$ or cerebr\$ or cerebell\$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage\$ or hemorrhage\$ or haematoma\$ or hematoma\$ or bleed\$)).tw.
5. hemiplegia/ or exp paresis/
6. (hemipleg\$ or hemipar\$ or paresis or paretic).tw.
7. or/1-6
8. carers/ or friends/ or exp parents/ or spouses/ or visitors to patients/
9. home nursing/ or community networks/ or exp parent-child relations/ or exp interpersonal relations/
10. family/ or exp family characteristics/ or family relations/ or intergenerational relations/
11. family therapy/ or family nursing/ or family health/
12. (carer\$ or carer\$ or care giver\$ or care-giver\$).tw.
13. (family or families or spous\$ or parent or parents or father\$ or mother\$ or friend or friends or husband\$ or wife or wives or partner or partners).tw.
14. ((home or communit\$) adj5 care).tw.
15. (home-based or community-based).tw.
16. home nursing.tw.
17. ((non-professional or non professional or informal) adj5 (care or nursing)).tw.
18. (next of kin or relatives).tw.
19. or/8-18
20. 7 and 19
21. limit 20 to humans
22. Randomized Controlled Trials/
23. random allocation/
24. Controlled Clinical Trials/
25. control groups/
26. clinical trials/
27. double-blind method/
28. single-blind method/
29. cross-over studies/
30. Therapies, Investigational/

31. Research Design/
32. Program Evaluation/
33. evaluation studies/
34. randomized controlled trial.pt.
35. controlled clinical trial.pt.
36. clinical trial.pt.
37. evaluation studies.pt.
38. random\$.tw.
39. (controlled adj5 (trial\$ or stud\$)).tw.
40. (clinical\$ adj5 trial\$).tw.
41. ((control or treatment or experiment\$ or intervention) adj5 (group\$ or subject\$ or patient\$)).tw.
42. (quasi-random\$ or quasi random\$ or pseudo-random\$ or pseudo random\$).tw.
43. ((control or experiment\$ or conservative) adj5 (treatment or therapy or procedure or manage\$)).tw.
44. ((singl\$ or doubl\$ or tripl\$ or trebl\$) adj5 (blind\$ or mask\$)).tw.
45. (coin adj5 (flip or flipped or toss\$)).tw.
46. latin square.tw.
47. versus.tw.
48. (cross-over or cross over or crossover).tw.
49. (assign\$ or alternate or allocat\$ or counterbalance\$ or multiple baseline).tw.
50. controls.tw.
51. (treatment\$ adj6 order).tw.
52. or/22-51
53. 21 and 52

EMBASE search strategy¹²

1. Clinical trial/
2. Randomized controlled trial/
3. Randomization/
4. Single blind procedure/
5. Double blind procedure/
6. Crossover procedure/
7. Placebo/
8. Randomi?ed controlled trial\$.tw.
9. Rct.tw.
10. Random allocation.tw.
11. Randomly allocated.tw.
12. Allocated randomly.tw.
13. (allocated adj2 random).tw.
14. Single blind\$.tw.
15. Double blind\$.tw.

16. Placebo\$.tw.
17. Prospective study/
18. or/1-17
19. Case study/
20. Case report.tw.
21. Abstract report/ or letter/
22. 19 or 20 or 21
23. 18 not 22
24. exp cerebrovascular accident/
25. exp STROKE/
26. exp brain ischemia/
27. 24 or 25 or 26
28. exp CARER/
29. exp home care/
30. 28 or 29
31. 23 and 27 and 30

CINHAL search strategy¹²

- S24. S19 and S23
- S23. S20 or S21 or S22
- S22. (MH "Carer Home Care Readiness (Iowa NOC)")
- S21. (MH "Age Specific Care")
- S20. (MM "Carers")
- S19. S12 and S18
- S18. S13 or S14 or S15 or S16 or S17
- S17. "cerebrovascular event"
- S16. "cerebrovascular accident"
- S15. "cerebrovascular disorder"
- S14. "stroke" OR stroke/exp OR MH stroke
- S13. "cerebrovascular attack"
- S12. S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 g
- S11. TX allocat* random*
- S10. (MH "Quantitative Studies")
- S9. (MH "Placebos")
- S8. TX placebo*
- S7. TX random* allocat*
- S6. (MH "Random Assignment")
- S5. TX randomi* control* trial*
- S4. TX ((singl* n1 blind*) or (singl* n1 mask*)) or TX ((doubl* n1 blind*) or (doubl* n1 mask*)) or TX ((tripl* n1 blind*) or (tripl* n1 mask*)) or TX ((trebl* n1 blind*) or (trebl* n1 mask*))
- S3. TX clinic* n1 trial*
- S2. PT Clinical trial
- S1 (MH "Clinical Trials+")

Glossary

Allocation concealment	Is the application of a randomisation sequence. How the randomisation sequence is applied when participants are enrolled a randomised controlled trial is of critical importance. Ideally, those who have the responsibility for enrolment, obtaining consent and treatment allocation should be completely unaware of the next treatment assignment in the sequence. Ignorance of the next treatment assignment protects those with responsibility for enrolling and allocating participants from being influenced by foreknowledge of the next assignment. The purpose of allocation concealment is to protect against selection bias. Good allocation concealment mechanisms include central randomisation (including telephone, telephone or pharmacy controlled randomisation systems) or sequentially numbered opaque sealed envelopes or sequentially numbered drug containers of identical appearance.
Applicability	The extent to which the results of a study or review can be applied to the target population for a study or systematic review.
Attrition bias	When a study is prospective in nature and data collection occurs at one or more points in time, it is possible for some participants to leave the study before the study is complete. The attrition of the original study sample can occur in experimental and non experimental study designs where there is baseline and follow-up data collection at different time points. Attrition means that outcome data are not available for the original study sample. Common reasons for attrition include loss to follow-up and withdrawal. The result of attrition is that the effect estimates may become biased.
Bias	Errors in the estimation of the occurrence of disease. Errors (bias) can occur by chance (random error) or as a result of <i>systematic</i> errors in the design and conduct of a study. Systematic error can occur at different stages in the research process, for example,

	in the selection of participants, in the participation of individuals in the study, in the measurement of participants, in the collection, analysis, interpretation, publication or review of research data. For examples see <i>Selection bias, Performance bias, Attrition bias, Information bias, Detection bias, Reporting Bias, Confounding, Publication bias</i> .
Blinding	The practice of keeping study personnel, study participants and outcome assessors ignorant to which intervention a participant received. The purpose of 'blinding' or 'masking' is to protect against performance bias, attrition bias and detection bias.
Care	The term care refers to the provision of what is necessary for the health, welfare, maintenance, or protection of another individual in illness, frailty or disability.
Care recipient	<i>Care recipient:</i> The term care recipient refers to the individual in illness, frailty or disability who is in receipt of care from an informal carer.
Case-control study	A non experimental study which recruits people who have the disease or health outcome of interest (cases) and an unaffected group (controls). Their exposure to factors of interest (such as consumption of particular drug for example Thalidomide) is compared. If the people who have disease have greater exposure than the control group then it may be inferred that there is a causal relationship between the factor and the risk of developing disease or health condition.
Causal relationship	Describes the relationship between one variable (A) and a second variable (B) when it can be established that (A) causes B). <i>Randomised controlled trials</i> are the best way to ascertain causality. Proving that there is a cause and effect requires certain key criteria to be met (such as does -response, temporality, biological plausibility). Demonstrating an association between two variables does not show a cause and effect relationship.
Cluster	A study in which treatments or interventions are

Randomisation	randomly allocated to groups of individuals (for example, patients in hospital wards, general practitioner practices).
Cochrane Library	The Cochrane Library consists of a regularly updated collection of evidence-based health care databases including the Cochrane Database of Systematic Reviews (Reviews of <i>randomised controlled trials</i> prepared by the <i>Cochrane Collaboration</i>).
Cohort	A group of people sharing some common condition or characteristic (for example, a birth cohort with the same year of birth in common, patients with the same disease, a cohort of carers has the experience of providing informal care in common).
Cohort study	A non experimental study which recruits people who are free of the disease and who are followed up over time to see what happens. A cohort study may consist of one cohort that is diverse with regards to exposure history such as a cohort of nurses or a cohort of doctors. Cohort studies may also include two or more groups of people who differ with regards to the extent of their exposure to a putative cause of disease. For example tooth decay in children who are exposed to fluoridated drinking water compared to children who are not exposed to fluoridated drinking water.
Comorbidity	Co-existence of one or more diseases in the people being studied in addition to the health problem that is under investigation.
Confounding, confounder or confounding factor	Is a mixing of effects. Confounding occurs when an association between and exposure (for example coffee consumption) and a disease (for example coronary heart disease) is being studied and another exposure (for example smoking) exists in the population under study that is associated with the health outcome or disease being studied (coronary heart disease). A confounding factor may falsely show an apparent association between the study variables where no real association exists. Equally a confounding factor may conceal a real association. If

	confounding factors are not measured and controlled for, bias may result in the conclusion of the study.
Consecutive sample	Sample for a study is made up of an entire population and is recruited over a long enough period to account for any temporal variations. Consecutive samples can reduce selection bias and volunteerism.
Convenience sample	Sample for a study is made up of people who meet the entry criteria and are easily accessible to the study investigators. One type of convenience sample is a <i>consecutive sample</i> .
Detection bias	Systematic differences in how study outcomes are assessed or determined.
Disability	Limitations in physical or mental function, caused by one or more health conditions, in carrying out socially defined tasks and roles that an individual is generally expected to be able to do.
Cross sectional study	Cross sectional studies collect data all at the same time. Respondents are usually only contacted once. They are descriptive studies but can be used to assess associations between variables. Examples of cross sectional studies include Census and national surveys. Cross sectional studies are often referred to as prevalence studies.
Detection bias	Systematic differences between groups in how outcomes are determined ³²¹ .
Disabling condition	The term <i>disabling condition</i> refers to any physical or mental health condition that can cause disability ⁷ .
Effects	The outcome of a given cause for example human immunodeficiency virus (HIV) (outcome) is the effect of sharing needles for drug use ²¹⁰ . Effect can also mean the change in population characteristics that is caused by a factor (for example a behaviour (e.g., smoking); a disease (e.g., HIV); a trait (e.g., a genotype); an intervention (e.g., educational programme) being at one level or another ²¹⁰ .
Epidemiology	Study of the frequency, distributions and

	determinants of diseases in populations.
Experimental intervention	An intervention (for example, a training programme) being studied to see if it has an effect on the course or outcome of a health condition or outcome of interest.
Exposure	The term exposure refers to a factor or characteristic which may produce or cause an effect. For example sharing needles for drug use (exposure) may cause the human immunodeficiency virus (HIV) (effect) ²¹⁰ .
External validity	The extent to which the results of a study apply to people in non-study situations, for example, in routine clinical practice. Also known as <i>generalisability</i> .
Forest plot	A graphical display of results from individual studies and meta-analysis. Results are presented as effect estimates and confidence intervals. Results are presented on a common scale, which allows for visual comparison of results and examination of the degree of <i>heterogeneity</i> between studies.
Funnel plot	Funnel plots are simple scatter plots. They are a graphical representation of effects of an exposure estimated from separate studies on the horizontal axis against some measure of the study size on the vertical axis. <i>Publication bias</i> can lead to asymmetry in funnel plots.
Generalisability	The extent to which the results of a study apply to people in non-study situations, for example, in routine clinical practice. See also <i>external validity</i> .
Health condition	The term <i>health condition</i> includes <i>pathology</i> , or active disease, as well as <i>impairment</i> , which refers to losses of mental, anatomical, or physiological structure or function owing to injury, active disease, or residual losses from formerly active disease ⁷ .
Heterogeneity	The term is used in <i>meta-analyses</i> and <i>systematic reviews</i> when the observed intervention effect varies across studies included in a meta-analysis. Estimates of effect can vary in both the size and direction of effect with some studies suggesting a beneficial

	<p>effect and others suggesting an adverse intervention effect. Such <i>varied estimates</i> may occur as a result of differences between the included studies in terms of methods, study populations, outcomes measured and definition of variables during follow-up.</p>
Intention to treat analysis	<p>An analysis of a randomised controlled trial where study participants are analysed according to the group to which they were originally randomly assigned, regardless of whether or not they had completely complied with the treatment they were assigned to receive, crossed over to the comparator treatment arm and received that instead or withdrew from the study. Intention-to-treat analyses are important in assessment of the effects of interventions as they provide a realistic assessment of how effective a treatment may be in clinical practice where withdrawal from treatment and taking alternative treatments is likely to be normal.</p>
Informal carer	<p>The term carer refers to an individual who provides what is necessary for the health, well being, maintenance and protection of another person in illness, frailty or disability. The individuals who provide care do not receive remuneration for the care they provide.</p>
Information bias	<p>Measurement errors in the collection of information needed for analysis. There are many sources of information bias and the effects of each vary. One type of information bias in retrospective case-control studies is recall bias. Recall bias is differential recollection of information with regards exposure by cases and controls. This form of information bias is known as differential misclassification. Recall bias can either over or under estimate the effect of an exposure. Examples of non differential misclassification include wrongly classifying people who are unexposed (such as smokers not admitting to smoking). Other sources of information bias include: inaccurate observation by a study investigator; equipment imprecision; and the use of exposure-assessment instruments or rating scales which are not fit purpose.</p>

Internal validity	Refers to the integrity of the study design.
Intervention	Healthcare action intended to benefit the study participant i.e. stroke survivor or carer, for example, training programme, psychological input etc.
Matching	Individual participants in the unexposed groups are selected in a constant ratio to equal the characteristics of the exposed group in factors which are known to be confounders such as age, sex or socio economic status. The result of matching is that the distribution of matching variables is similar in the exposed and unexposed groups and as a consequence these factors are removed as a source of confounding.
Mean difference	A measure of the absolute difference between the mean values in two groups in for example a cohort study or a clinical trial.
Meta-analysis	Results from a collection of primary studies addressing the same or similar question about the effects of an intervention are pooled, using statistical techniques to synthesise their findings into a single summary estimate of a treatment effect. Where studies are not sufficiently similar for example, because of differences in the study populations, interventions or in the outcomes measured, it may be inappropriate or even misleading to statistically pool results in this way.
Meta-regression	Is an investigation into how a categorical study level characteristic is associated with the intervention effects in a meta-analysis ¹²⁷ . Examples of study level categorical characteristics which may be appropriate for meta-regression include: adequate allocation sequence generation or not, adequate allocation concealment or not or adequate or inadequate blinding of study personnel or participants. Meta-regression is an extension of sub-group analysis. A minimum of ten studies are required for meta-regression.
Methods	The overall approach to study design, study conduct and study analysis.

Methodological quality	The extent to which a study has conformed to recognised good practice in the design and conduct of its research methods.
Odds ratio	Is a measure of the odds of an event/disease occurring.
Performance bias	Systematic differences in care provided apart from the intervention being evaluated or in exposure to factors other than the factors of interest ³²¹ .
Probability sample	A study sample in which all people in a population have had an equal probability of being selected.
Publication bias	Studies with suggesting a large effect size of a beneficial intervention effect are more likely to get published than those with non-significant results. Systematic reviews based on published data only are likely to be biased. Publication bias is assessed by a funnel plot.
Random allocation	When an experiment is in the design process, randomization is a consideration when a subject is being assigned to a group or when a group is being assigned to a treatment. Each unit (i.e., person, group) is assigned treatment using a random method of assignment such as random number tables, repeated coin tossing, drawing lots or computer generated random numbers. Random means that each individual (or each unit in the case of <i>cluster randomisation</i>) being entered into a study has the same chance of receiving each of the possible interventions. By assigning treatments to experimental units at random, systematic error or bias is removed and any association between treatment assignment it produces and the extraneous factors will be random.
Randomisation sequence generation	Randomisation sequence is the method used to generate an unpredictable sequence of treatment assignments. Adequate methods for generating a randomisation sequence include: random number tables, repeated coin tossing, drawing lots or computer generated random numbers.

Randomised controlled trial	An experimental design in which the effects of two or more interventions are compared by randomly assigning the intervention to participants. <i>Options for comparator groups include no intervention or control intervention.</i>
Reporting bias	The reporting of research findings based on the nature and direction of results. For example, studies in which interventions are shown to have no benefit are not always published, meaning that not all relevant and important evidence on the effects of an intervention are available.
Risk difference	Is a measure of the probability of an event/ disease occurring.
Risk factor	A risk factor (such as age, sex) is a variable associated with an increased risk of disease or outcome of interest. There can be an association between a risk factor and a disease/ ill health but this does not imply a causal relationship.
Reliability (measurement)	Refers to a method of measurement that consistently gives the same results for a particular setting, population and purpose.
Risk ratio	Is a measure of probability of an event/disease occurring.
Sample	The subset of a target population that has agreed to participate in a study.
Sampling	Refers to the methods used to select participants for inclusion in a study.
Selection bias	In a randomised controlled trial selection bias refers to systematic differences in the baseline groups that are being compared ³²¹ . In a non experimental study selection bias refers to systematic differences between the characteristics of people who are selected or have agreed to participate from those people who are or have not.
Standardised mean difference	A measure of the absolute difference between the mean values in two groups in for example a cohort

	study or a clinical trial. See also mean difference.
Stratification	An analyses in which participant data are split into defined strata such as stratifying by age (age strata). Effect estimates can then be examined within and across well defined homogenous strata of a confounding variable (such as age, sex or ethnic group). Stratification can increase the efficiency of a study by controlling for confounding. However, stratification is limited by study size and it is difficult to stratify for many factors at the same time.
Sub group analysis	An analysis in which participant data are split into a defined subset of participants in order to make comparisons between them. Examples of sub group analyses include subsets of participants (males and females, age categories), subsets of studies (geographical location). Sub group analyses are valuable in investigating heterogeneity.
Systematic review	A review focused on a research question in which evidence from multiple primary studies addressing the same or a similar question are identified, appraised and synthesised in a methodical way according to explicit, objective and reproducible predetermined criteria. May or may not include a <i>meta-analysis</i> .
Validity (measurement)	The degree to which a measure assesses what it claims to measure for a particular setting, population and purpose.

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