Exploring Anxiety, Depression and their Correlates Among Implantable Cardioverter Defibrillator (ICD) Recipients and People with Chronic Heart Failure

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Submitted in partial fulfilment of the requirements for the degree of
Doctorate in Clinical Psychology

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Acknowledgements

Many thanks to Professor Hamish McLeod, Dr Katie Robb and Dr John Sharp for their supervision and support throughout the development and completion of the project.

My sincere gratitude to Dr Ross Campbell who gave permission to access a wealth of data from a cohort of people living with heart failure. This allowed me to progress through the DClinPsy program despite the disruptions to my original project as a result of the COVID-19 pandemic. I would also like to thank staff at the Robertson Data Centre for Biostatistics for efficiently reviewing and approving data-outputs during the secondary analysis process.

Thanks to Paul Cannon for providing invaluable guidance on developing electronic strategies for systematic reviews.

A special mention to my close friends and family, for their continued support and for providing a safe space to 'vent' during the challenges of the last three years.

Foreword

The original project titled ‘An investigation into the socio-demographic, clinical and psychological variables associated with psychological adjustment and health-related quality of life in Implantable Cardioverter Defibrillator (ICD) recipients’ (See original project proposal in Appendix 2.1, p.142-158) had to be abandoned.

An ethics application based on this proposal had been completed and was due to be submitted on the Integrated Research Application System (IRAS). Nevertheless, this coincided with the first wave of the COVID-19 pandemic.

Unfortunately, the original project could not go ahead as planned because data collection would have involved attending outpatient clinics to recruit ICD-recipients. During the first wave of the pandemic, some health boards suspended routine clinical activity and a proportion of the health care staff identified to facilitate the author’s access to participants had been redeployed. Additionally, the target population included individuals with various cardiac conditions and physical health comorbidities. Therefore, potential participants fell under the ‘clinically vulnerable’ group, who were asked to shield at home and avoid unnecessary social contact between March and July 2020.

As a result of these circumstances, it was agreed by the author and research supervisors to abandon the original project. The author’s field and research supervisors - Dr John Sharp and Professor Hamish McLeod facilitated access to an existing data set for secondary analysis. This resulted in the development of an alternative project titled ‘Trajectories of Anxiety and Depression in Patients with Chronic Heart Failure’, which is featured in chapter two. The author had significant intellectual input in the direction of this project by completing a research protocol and contributing to the statistical analysis plan. See Appendix 2.2, p.159-162, for a summary of the project protocol and Appendix 2.3, p.163, for an overview of the author’s intellectual contribution to the development of the project.

Chapter One: Systematic Review

Factors Influencing Anxiety and Depression in Implantable Cardioverter Defibrillator (ICD) Recipients: A Systematic Review

Prepared in accordance with the author requirements for submission to the Journal of Clinical Nursing (Appendix 1.1, p.126).

Abstract

Aims and Objectives: To systematically review factors influencing anxiety and depression in implantable cardioverter defibrillator (ICD) recipients.

Background: An ICD is a device used to prevent life-threatening ventricular arrhythmias. While the ICD is accepted by most recipients: a considerable number of patients experience distress following implant. The socio-demographic, clinical, ICD-specific and psychosocial factors associated with distress in ICD-recipients has received increasing attention.

Methods: Six electronic databases (Applied Social Science Index and Abstract, CINAHL, EMBASE, Medline, Psychology and Behavioral Sciences Collection and PsycINFO) were searched on the 24/07/2020. Additional papers were identified by hand searching relevant journals, forward citation searching and reviewing the reference lists of included studies. This review was limited to studies on adult patients who received a transvenous or automatic ICD or ICD with cardiac resynchronisation therapy for primary or secondary prevention purposes. Other inclusion criteria were peer reviewed quantitative papers published in English from January 2014 to July 2020, which examined factors influencing anxiety and depression. The quality of the papers was rated using the Crowe Critical Appraisal Tool.

Results: Anxiety and depression were linked to socio-demographic factors (female sex, younger age, living alone), clinical factors (heart failure, coronary heart-disease or history of emotional distress/psychotropic medication use), ICD-specific factors

(elevated ICD-related concerns, low ICD knowledge, negative treatment expectations), and psychosocial factors (avoidance, perceived control, Type D personality and optimism).

Conclusions*:* All papers suffered from methodological limitations and the findings should be interpreted with caution. Future research employing prospective longitudinal designs with controls for confounding factors is required to understand the relationship between socio-demographic, clinical, ICD-specific and psychosocial factors and distress in ICD-recipients over time.

Relevance to clinical practice: Results demonstrated a relationship between elevated ICD-related concerns and increased distress in ICD-recipients. Routine screening for ICD-related concerns may identify patients at risk of anxiety and depression post ICD-implant.

Keywords: anxiety, depression, implantable cardioverter defibrillator

Introduction

An implantable cardioverter defibrillator (ICD) is an electronic device for treating life-threatening ventricular arrhythmias (VAs) and preventing sudden cardiac death (Magyar-Russell et al., 2011). The ICD is implanted under the skin, and continuously monitors an individual's heart rhythm through electrodes. If an abnormal rhythm occurs, the ICD delivers electrical pulses to shock the heart to restore normal rhythms. ICDs are indicated for individuals at risk for VAs (primary prevention) or survivors of life-threatening VAs resulting in cardiac arrest (secondary prevention) (Hauer et al., 2001).

Research suggests ICDs are more effective than pharmacological therapy in preventing sudden cardiac death (Akel & Lafferty, 2017). The ICD is accepted by most recipients; however, some patients experience anxiety, depression, and reduced quality of life (QoL) after implant (Pedersen et al., 2005). Research has reported significant inter-study variance in the prevalence rates of depression (24% to 33%) and anxiety (24% to 88%) in ICD-recipients (Camm et al., 1999). Some have suggested this variability is due to use of different measures to assess anxiety and depression (Magyar-Russell et al., 2011).

A systematic review found studies using clinical interviews to assess anxiety and depression indicated between 11-26% of ICD participants' met criteria for an ‘anxiety or depressive disorder’ (Magyar-Russell et al., 2011). While rates of elevated symptoms (based on self-report measures) ranged from 8-63% for anxiety and 5-41% for depression (Magyar-Russell et al., 2011).

ICD-recipients with anxiety and depression are at increased risk of mortality and hospital re-admission (Berg et al., 2019) so an understanding the risk factors for these psychological responses is needed. There are several reasons hypothesised for elevated distress in ICD-recipients including worry about the seriousness of the heart condition and unpredictability of receiving device shocks (Conti & Sears, 2001). The experience of device shock can be distressing, and the physical sensations caused by the discharge can be painful and have been likened to a 'kick in the chest' (Ahmad et al., 2000). This experience can lead to a conditioned response marked by avoidance of activities associated with ICD shock, fuelled by anticipatory anxiety of receiving shocks (Sears & Conti, 2002).

A body of research has investigated the demographic, clinical and psychosocial factors associated with increased psychological distress in ICD-recipients. One review article indicated socio-demographic factors including younger age (<50), female sex, and unemployment negatively impacted the psychological status of ICD-recipients (Kajanová, Bulava & Eisenberger, 2014). Two reviews reported clinical factors, including the number of ICD shocks received, presence of co-morbid health difficulties (e.g., heart failure) and time since implant are associated with anxiety and depression in ICD-recipients (Freedenberg, Thomas & Friedmann, 2011; Kajanová et al., 2014).

Research examining the relationship between ICD-specific factors and distress including time since implant, receipt of device shock and ICD indication has produced mixed findings. Some research indicates ICD-recipients' levels of psychological distress reduces during the first year after implant (Amiaz et al., 2017). Others have not found consistent decreases over time (Van den Broek et al., 2013). Studies employing

prospective and longitudinal designs are required to examine the trajectories of anxiety and depression in ICD-recipients over time (Van den Broek et al., 2010).

Similarly, the ICD shock literature is inconsistent, with only 10 out of 29 studies finding a significant relationship between device shock and emotional distress (Manzoni et al., 2015). Conclusions about the relationship between device shock and distress cannot be drawn due to heterogeneity in the studies' design, methodology and measures used to assess distress (Manzoni et al., 2015). Studies also suffer from limitations including collecting shock data via self-report, which is susceptible to recall bias, with 29% of ICD-recipients underestimating and 16% overestimating the number of shocks received (Ahmad et al., 2000).

The reason for ICD-implant may influence emotional distress, with primary prevention ICD-recipients reporting heightened anxiety compared to secondary prevention patients (Rahmawati et al., 2016). It is argued secondary prevention recipients appraise risk of cardiac death as higher due to previous experience and therefore view their ICDs as lifesaving (Rahmawati et al., 2016). Conversely, primary prevention patients have not experienced life-threatening cardiac event(s) and may struggle to accept why they need the ICD, resulting in adjustment difficulties. Data has also shown secondary ICD indication independently predicted depression in male ICD-recipients, while primary prevention indication was associated with anxiety (Miller, Thylén & Moser 2016). Nevertheless, findings are inconsistent as some researchers found no association between ICD indication and ICD-recipients' distress (Habibović, et al., 2017b; Thylén et al., 2014).

The literature has also examined the relationship between psychological factors and emotional distress, showing Type D personality (defined as the tendency to experience increased negative affect while supressing these emotions due to a fear of disapproval from others) is associated with heightened anxiety and depression in ICD-recipients (Denollet & Van Heck, 2001; Kajanová et al., 2014). Additionally, research has supported the predictions of psychological models including the self-regulation model of adjustment to illness (Leventhal, Meyer & Nerenz, 1980), which highlights the role cognitive illness representations play in emotional adjustment. For example, one study found illness representations including low perceived control was independently associated with elevated anxiety and depression in ICD-recipients (Israelsson et al., 2018).

ICD-specific cognitive appraisals have also been identified as influencing distress. ICD-related concerns (e.g., worry about the ICD discharging) have been described as universal and are measured using the ICD Patient Concerns (ICDC) questionnaire (Pedersen et al., 2005). Data has shown ICD-related concerns were an independent determinant of psychological distress after controlling for the number of shocks received (Pedersen et al., 2005). A multicentre study of 334 ICD-recipients found ICD-related concerns and low perceived control mediated the relationship between device shock and emotional distress (Lee et al., 2020). Accordingly, psychological factors including ICD-related concerns and perceptions of control may have a more substantial impact on ICD-recipients' distress, compared to clinical factors including device shock (Lee et al., 2020; Pedersen et al., 2005).

Aims

Given the mixed findings in previous studies, the aim of this review is to identify factors influencing anxiety and depression in ICD-recipients. This has the potential to help clinicians identify ICD-recipients at risk of less favorable outcomes and elucidate modifiable factors that could be targeted in the development of supportive interventions for ICD-recipients.

Review Question

1. What socio-demographic, clinical, ICD-specific and psychosocial factors influence anxiety and depression in ICD-recipients?

Method

Electronic Search Strategy

Six electronic databases (Applied Social Science Index and Abstracts, CINAHL, EMBASE, Medline, Psychology and Behavioral Sciences Collection and PsycINFO) were searched on the 24/07/2020. Filters were used to limit search results to those published in journals in English. Additionally, as a previous descriptive review of factors influencing the psychological status of ICD-recipients was published in 2014 (Kajanová, Bulava & Eisenberger, 2014) a filter was used to limit search results to papers published from January 2014 until July 2020. All identified titles were screened for relevance and included or excluded according to the inclusion/exclusion criteria detailed below.

Search Terms

The search terms varied slightly depending on the requirements of the different databases use of index/subject headings and Boolean operators. See Appendix 1.2, p.127-133 for full details of the search strategy. The following search terms were used to search Psychology and Behavioral Sciences Collection (EBSCO HOST):

1. SU (DE "ANXIETY") OR (DE "ANXIETY disorders") OR (DE "PSYCHOLOGICAL stress") OR (DE "DISTRESS (Psychology)") OR (DE "MENTAL depression") OR (DE "ADJUSTMENT disorders") OR (DE "AFFECTIVE disorders") OR (DE "PSYCHOLOGICAL adaptation") OR (DE "PSYCHOLOGICAL well-being") OR (DE "DISTRESS (Psychology)") OR (DE "PSYCHOLOGICAL stress") OR (DE "PATHOLOGICAL psychology") OR (DE "MENTAL health")
2. TI (anxi* or depress* or mood disorder* or emotion* or psych* or (mental n2 status) or (affective n2 disorder*) or (low n2 mood) or dysthymia or distress or stress or (mental n2 health) or (mental n2 illness) or (mental n2 wellbeing) or (mental n2 disorder*) or (psychological n2 adjustment) or (emotional n2 adjustment) or (adjustment n2 disorder) or (emotional n2 adaptation)) OR AB (anxi* or depress* or mood disorder* or emotion* or psych* or (mental n2 status) or (affective n2 disorder*) or (low n2 mood) or dysthymia or distress or stress or (mental n2 health) or (mental n2 illness) or (mental n2 wellbeing) or (mental n2 disorder*) or (psychological n2 adjustment) or (emotional n2 adjustment) or (adjustment n2 disorder) or (emotional n2 adaptation))

3. S1 OR S2
4. SU "IMPLANTABLE cardioverter-defibrillators"
5. TI (((Implantable cardioverter defibrillator or ((implantable or internal or automatic or automated) n2 (cardioverter or defibrillator)) or AICD or ICD).)) OR AB (((Implantable cardioverter defibrillator or ((implantable or internal or automatic or automated) n2 (cardioverter or defibrillator)) or AICD or ICD).))
6. S4 OR S5
7. S3 AND S6

Hand searches were completed in two stages between July 2020 until October 2020. First the reference sections within all papers identified for inclusion were searched. Second, forward citation searches of included articles were conducted to identify other potentially relevant articles overlooked by the electronic searches.

Inclusion Criteria

- Studies written in English in peer reviewed journals.
- Quantitative studies (randomised controlled trials (RCTs), pseudo-randomised trials, cohort, cross-sectional and prospective studies, case control, observational and descriptive studies).
- Studies using validated questionnaires to assess anxiety and depression in ICD-recipients (>3 months after ICD) implantation.
- Studies including individuals ≥ 18 years with implantation of a transvenous or automatic ICD or ICD with cardiac resynchronization therapy (CRT-D).
- Included individuals who received their ICD for primary or secondary prevention.
- Included ICD-recipients with heart failure, atrial fibrillation, coronary heart disease, myocardial infarction, cardiomyopathy, and congenital heart conditions.

Exclusion Criteria

- Studies published before 2014.
- Studies where the primary aim was to validate assessment tools for anxiety or depression.
- Studies only including measurements of anxiety and depression pre-ICD implantation or in early stages post-ICD implantation (<3 months post-implant).
- Qualitative studies, literature reviews, book chapters, systematic reviews, conference abstracts, clinical guidelines, editorials or reports of expert opinions.
- Studies investigating ICD-recipients <18 years old, those who had not yet received their ICD or participants with a 'wearable' or subcutaneous ICD.

Study Selection

The electronic search generated 6159 papers**,** of which 2274 were duplicates. The author screened the titles and abstracts of the remaining 3885 papers against the inclusion/exclusion criteria, of which 3835 were irrelevant. The full-text of 50 papers were reviewed and 31 studies were excluded. In cases where the author was unsure whether a paper met the inclusion criteria a second reviewer screened the paper independently from the author. The full-text of four papers were assessed by the second reviewer, and differences of opinion were resolved through discussion. Disagreements were minimal (i.e., the reviewers had reached the same decision to include three out of the four papers). One disagreement occurred, in which the second reviewer accepted one paper which did not meet the inclusion criteria (e.g., the paper only included a measure of anxiety or depression <3 months after ICD-implantation). A total of 19 papers were identified for inclusion. See Figure 1 for an overview of the selection process and Appendix 1.3, p.134 for details of the electronic search results.

Data extraction

The data of included papers were extracted using a modified version of the Joanna Briggs Institute-Meta Analysis of Statistics Assessment and Review Instrument, data extraction tool used in a similar review (Wong, et al., 2012). See Appendix 1.4, p.135-137.

Quality Appraisal

The quality of the 19 papers was assessed using the Crowe Critical Appraisal Tool (CCAT) (Crowe, 2013). The CCAT contains eight items assessing reporting and methodology including: preliminaries, introduction, design, sampling, data collection, ethical issues, results and discussion (See Appendix 1.5, p.138-139). Each category is scored on a scale of zero (lowest) to five (highest) and a total score (out of 40) and corresponding % is obtained. For this study, a total score rating of 0-50% was judged as low, 51-75% moderate, and 76-100% high quality. A second researcher independently rated a random sample of three papers. Disagreements about ratings were minimal (all category scores were within 1 point), with any discrepancies being resolved through discussion until agreement was achieved.

Results

The nineteen included studies are summarised in Table 1.

Figure 1. PRISMA Flow Diagram of Selection Process

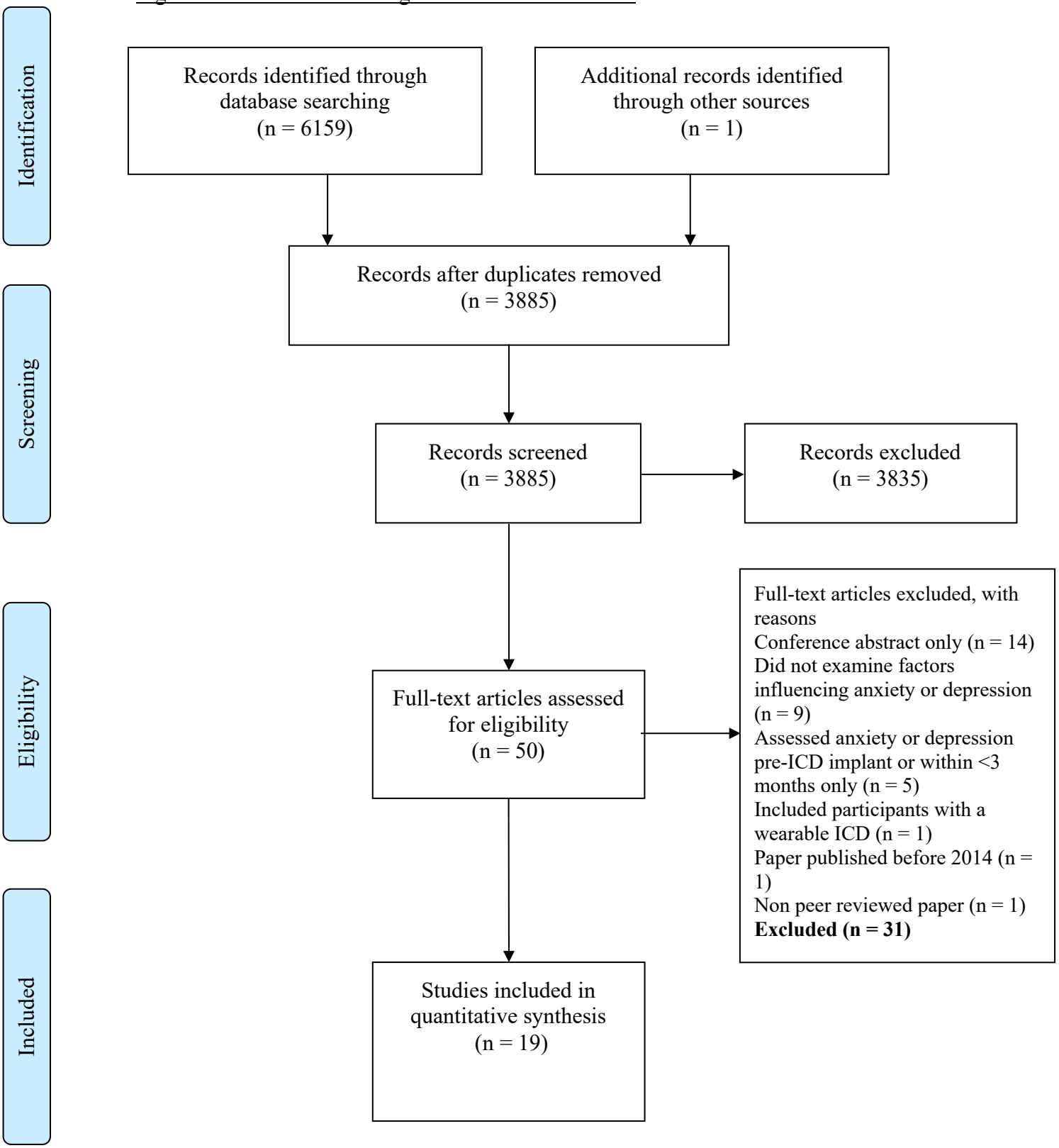

Table 1: Overview of Studies and Summary of Findings

Number	Authors, year, country	Design	Participants	Primary Aims	Measures	Main Findings	Quality Rating %
1	Amiaz et al., 2016 Israel	Retrospective cross-sectional study	95 ICD-recipients 80 (84%) were male Mean age: 66	To determine the prevalence of anxiety and depression in ICD-recipients	MINI HAM-D HAM-A Recipients' attitudes to ICD were collected using a visual analogue scale	ICD-recipients with higher NYHA class, co-morbid HF, and had a coronary artery bypass graft had higher HAM-D scores Attitudes towards the ICD were positively associated with HAM-D scores HAM-D scores were negatively associated with objective device shocks, but shocks did not correlate with depression after controlling for NYHA class and co-morbid HF	53%

Number	Authors, year, country	Design	Participants	Primary Aims	Measures	Main Findings	Quality Rating %
2	Amiaz et al., 2017 Israel	Longitudinal study of consecutively implanted ICD-recipients Measures assessed at baseline (pre-surgery), 3-months and 12-months post-implant	158 ICD-recipients at baseline, 142 at 3-month and 141 at 12-month follow-up 134 (85%) were male Mean age: 64	To identify the rate of new onset anxiety and depression in ICD-recipients	MINI HAM-D HAM-A	ICD-recipients with a history of mental health difficulties and psychotropic medication use had higher HAM-D scores Those with higher NYHA class reported higher depression at baseline, 3-month and 1-year follow-up Significant decrease in mean HAM-D scores observed between baseline, 3-months and 12-months post ICD-implant	63%

Number	Authors, year, country	Design	Participants	Primary Aims	Measures	Main Findings	Quality Rating %
3	Farahani et al., 2016 Iran	Cross-sectional study	115 ICD-recipients 88 (76.5%) were male Mean age: 59.85	To investigate the relationship between depression and clinical and socio-demographic factors in ICD-recipients	BDI	Male sex, frequency of device shock, higher number of hospital admissions, family history of depression, were associated with higher BDI scores	45%
4	Habibović, et al., 2017b Netherlands	Secondary analysis of data collected as part of the WEBCARE RCT (Habibović et al., 2017a) Measures assessed within 10 days post-implant, 3, 6 and 12-month follow-up	Analysis included 249 ICD-recipients 204 (82%) were male Mean age: 58.9	To investigate if different trajectories of anxiety & PTSD exist in ICD-recipients and to identify clinical, demographic and psychological characteristics associated with the trajectories	PDS GAD-7 PHQ-9 DS14	Type D personality, younger age, and increased depression at baseline were associated with heightened risk of anxiety at 12-months	65%

Number	Authors, year, country	Design	Participants	Primary Aims	Measures	Main Findings	Quality Rating %
5	Habibović et al., 2018 Netherlands	Secondary analysis of data collected from the WEBCARE RCT (Habibović et al., 2017a) Measures assessed at baseline and 12-months	Analysis included 171 ICD-recipients 138 (81%) were male Mean age: 59.6	To explore if baseline optimism scores are related to ICD-recipients self-reported depression, anxiety at 12-month follow-up	LOT GAD-7 PHQ-9 SF-12 DS14 CCI	After controlling for clinical, demographic and personality characteristics: baseline optimism was negatively correlated with anxiety and depression at 12-months Optimism was not significantly associated with change in depression and anxiety status, after controlling for baseline distress While controlling for clinical and demographic factors: CCI (comorbidities) and type D personality were associated with anxiety and depression at 12-months	70%
6	Ichikura et al., 2017 Japan	Cross-sectional design	Analysis included 119 ICD-recipients 86 (72.3%) were male Age range: 20-89	To determine the frequency of avoidance behaviours & investigate the relationship between avoidance and depression in ICD-recipients	BDI-II Avoidance questionnaire developed for a previous study (Lemon, Edelman & Kirkness, 2004)	Avoidance behaviours were significantly related to depression with an odds ratio of 1.31. Subgroup analysis (excluded participants with CRT-D) - results indicated living alone and avoidance were associated with heightened odds for depression	60%

Number	**Authors, year, country**	**Design**	**Participants**	**Primary Aims**	**Measures**	**Main Findings**	**Quality Rating %**
7	Israelsson et al., 2018 Sweden	Cross-sectional study Comparative design, ICD-recipient sample compared to general population data by a county council in Sweden (2006) Secondary analysis of data collected by study 15	Analysis included 990 cardiac arrest survivors with ICD Participants drawn from same sample as study 9, 14 and 15 772 (78%) were male Mean age: 65.6. General population sample: 1000 participants selected to match the age and sex of cardiac arrest survivors	To examine factors associated with HR-QoL in cardiac arrest survivors who received an ICD	EuroQol-5D-3 HADS ICDC CAS DS14	Female sex, ICD-related concerns, being unemployed, type D personality, lower perceptions of control, co-morbid health-issues were correlated with anxiety ICD-related concerns, co-morbid health-issues, type D personality and lower perceptions of control were associated with depression	58%

Number	Authors, year, country	Design	Participants	Primary Aims	Measures	Main Findings	Quality Rating %
8	Lee et al., 2020 Australia, Korea, & United States.	Multi-national cross-sectional study	334 ICD-recipients 251 (75%) were male Mean age: 59	To investigate if the correlation between ICD shocks and anxiety and depression was mediated by perceived control and ICD-related concerns	Brief Symptom Inventory (anxiety subscale) PHQ-9 ICDC CAS–Revised End-of-Life Issues in the ICD Patient Questionnaire	There was no direct effect of device shocks on anxiety and depression while controlling for age, ICD knowledge, and time since implant ICD shocks were indirectly associated with increased risk of anxiety and depression via the pathway of perceived control and ICD-related concerns (indirect effects on anxiety = 0.043, 0.060; indirect effects on depression = 0.073, 0.025)	63%

Number	Authors, year, country	Design	Participants	Primary Aims	Measures	Main Findings	Quality Rating %
9	Miller et al., 2016 Sweden	Cross-sectional study	Same sample as study 14 and 15 Analysis included 2771 ICD-recipients	To explore the differences in anxiety, depression and QoL between male and female ICD-recipients	HADS EQ-5D DS14 MSPSS 4-item CAS EOL-ICD Q Perceived ICD experience was rated on a 1–4-point scale	Low ICD knowledge, worse ICD experience, depression scores, low perceived control, low social support, device shock, total comorbidities, secondary prevention indication, Type D personality and younger age was associated with anxiety in males Low perceived control, type D personality, depression scores and worse ICD experience predicted anxiety in females Secondary ICD indication, older age, lower education status, longer time since ICD implant, low perceived social support, total comorbidities, low perceived control, anxiety scores, type D personality, and worse ICD experience predicted depression in males Poor social support, anxiety scores, Type D personality and total comorbidities predicted depression in females	63%

Number	Authors, year, country	Design	Participants	Primary Aims	Measures	Main Findings	Quality Rating %
10	Pedersen et al., 2018 Netherlands	Secondary analysis of data collected from the WEBCARE RCT (Habibović et al., 2017a) Measures were assessed at baseline (2 weeks post ICD-implant) and at 12-month follow-up	Analysis included 134 ICD-recipients 111 (83%) were male Mean age: 60	To investigate whether treatment expectations predicted depression at 12-months post ICD-implant	EXPECT-ICD PHQ-9 DS14	Negative treatment expectations (β = 0.202; p = .020) and baseline depression (β = 0.376; p < .001) emerged as independent predictors of depression at 12-month follow-up While controlling for sex, device shocks and co-morbid HF, negative treatment expectations (β = 0.180; p = .043), and baseline depression (β = 0.353; p < .001) emerged as significant predictors of depression at 12-month follow-up	63%
11	Rahmawati et al., 2016 Japan	Cross-sectional study Secondary analysis of data collected by Rahmawati et al (2013)	179 ICD-recipients 145 (81%) were male Mean age: 60.5	To determine if primary prevention ICD-recipients are at increased risk of psychological distress compared to secondary prevention patients	MOS STAI BDI IES-R WAICD	After controlling for clinical and demographic factors primary prevention ICD-recipients reported higher mean trait anxiety scores than secondary prevention recipients Primary prevention indication was correlated with trait anxiety and ICD-related concerns. Female sex was independently associated with depression	55%

Number	Authors, year, country	Design	Participants	Primary Aims	Measures	Main Findings	Quality Rating %
12	Rottmann et al., 2018 Netherlands	Secondary analysis of data collected from the MIDAS study, which was a longitudinal study of consecutively implanted ICD-recipients Measures assessed at baseline (1-day pre-implant), 10 days, 3, 6 and 12-month post-implant	Analysis included 286 ICD-recipients and their partners 227 (79.4%) were male Mean age: 59.3	To evaluate if perceived social support and clinical factors correlate with change in ICD-recipients and their partners anxiety and depression	HADS MSPSS	ICD-recipients & partners anxiety and depression levels decreased over time Higher ratings of social support were positively corrected reductions in anxiety and depression Device shocks, secondary ICD indication and symptomatic HF was associated persistent anxiety Having received ≥ 1 shock was associated with persistent depression	63%

Number	Authors, year, country	Design	Participants	Primary Aims	Measures	Main Findings	Quality Rating %
13	Starrenburg et al., 2014 Netherlands	Longitudinal study of consecutively implanted ICD recipients Measures assessed at: pre-implant, 2, 5, 8 and 12-months follow-up	300 ICD-recipients 247 (82.3%) were male Mean age: 62	To investigate the relationship between sex and anxiety, depression and HR-QoL while statistically adjusting for factors including clinical, demographic and psychological factors	HADS DS14 SF-36	After controlling for (ICD indication, shocks, ejection fraction, and co-morbid health conditions) females reported higher levels of anxiety than males over 12-month follow-up Males and females reported significant reductions in anxiety during 12-month follow-up Depression differed across time-points for females and males, with reductions seen two-months post-implant followed by return to pre-implant levels at 12-months	65%
14	Thylén et al., 2014 Sweden	Cross-sectional study	3067 ICD-recipients 2438 (79.5%) were male Mean age: 66	To identify characteristics associated with depression, anxiety and QoL in ICD-recipients	HADS EQ-5D ICDC	Symptoms of anxiety and depression were associated with HF, myocardial infraction, younger age, and living alone. Female sex was associated with higher probability of anxiety (β = 1.387; $p = .013$), elevated ICD-related concerns was the strongest predictor of anxiety (β = 4.224; $p < .001$), and depression (β = 1.387; $p < .001$)	68%

Number	Authors, year, country	Design	Participants	Primary Aims	Measures	Main Findings	Quality Rating %
15	Thylén et al., 2016 Sweden	Cross-sectional study	Same sample as study 14	To investigate whether the relationship between psychological distress and receiving ICD shock is statistically mediated by ICD-related concerns	HADS ICDC ICD shock experience was collected via self-report	ICD-recipients elevated ICD-related concerns were 4.98 times more likely to experience anxiety compared to those with low concerns Having ≥ 1 shock significantly predicted depression and anxiety The relationship between device shock and distress was mediated by high levels of ICD-related concerns, which explained 54% and 68% of the relationship between depression and anxiety respectively	65%
16	Varghese, Geller & Ohlow, 2019 Germany	Cross-sectional study using retrospective data collected from consecutively implanted ICD-recipients	423 ICD-recipients 342 (80.9%) were male Mean age: 68	Identify the incidence of phantom shocks (PS) in ICD-recipients & explore the link between PS and emotional distress	MLHFQ HADS	ICD-recipients who experienced PS reported higher anxiety scores and overall HADS score	48%

Number	Authors, year, country	Design	Participants	Primary Aims	Measures	Main Findings	Quality Rating %
17	Wong 2016 China	Secondary analysis of data collected in previous study (Wong et al., 2014) Cross-sectional study	139 ICD-recipients 107 (77%) were male 15.8% aged 50-59, 34.5% aged between 60–69, and 35.3% aged ≥ 70	To examine clinical, demographic, social and ICD-related factors associated with depression and anxiety in ICD-recipients	HADS SF-36v2 SSQ6	Being unmarried, having coronary heart disease, older age and being dependent for self-care was associated with depression. The model accounted for 21.6% of variance No clinical, demographic, social or ICD-related factors were associated with anxiety	48%
18	Wong 2018 China	Cross-sectional correlational study	57 ICD-recipients with history of CAD 40 (80.7%) were male Mean age: 63.04	To explore emotional distress in ICD-recipients with a history of coronary artery disease (CAD)	HADS SF-36v2	Female sex and self-care dependence were significantly correlated with anxiety Having diabetes and self-care dependence were significantly correlated with depression	48%

Number	Authors, year, country	Design	Participants	Primary Aims	Measures	Main Findings	Quality Rating %
19	Wong 2019 China	Cross-sectional study Secondary analysis of data collected by (Wong et al., 2014)	Same sample study 16 71 (ICD-only), 68 ICD with HF	To examine anxiety and depression and HR-QoL between ICD-recipients with and without HF	HADS SF-36v2	In ICD-recipients without HF: older age (≥ 60) and having obstructive airway disease was positively associated with depression while being unmarried and lower education was negatively associated with depression. Presence of coronary heart-disease was negatively correlated with anxiety In ICD-recipients with HF: older age (≥ 60), and having diabetes was positively associated with depression. Self-care independence and higher education level was negatively associated with depression. Self-care independence was negatively associated with anxiety	48%

Abbreviations: NYHA = New York Heart Association functional classification, HF = heart failure, PTSD = post-traumatic stress disorder, HR-QoL = health related quality of life, CRT-D = Cardiac Resynchronisation Therapy, CCI = Charlson Comorbidity Index, BDI = Beck Depression Inventory, Mini = Mini International Neuropsychiatric Interview, HAM-D = Hamilton Depression Scale, HAM-A = Hamilton Anxiety Scale, PDS = Posttraumatic-Stress Diagnostic Scale, GAD-7 = Generalised Anxiety Disorder Assessment, PHQ-9 = Patient Health Questionnaire, DS14 = Type D Personality Scale, LOT = Life Orientation Test, MSPSS = Multidimensional Scale of Perceived Social Support, HADS = Hospital Anxiety and Depression Scale, CAS = Control Attitudes Scale, SF-12 or 36 = Short-Form Health Survey 12 or 36 item, ICDC = ICD-related concerns questionnaire, MOS = Medical Outcomes Study, STAI = State-Trait Anxiety Inventory, IES-R = Impact of Event Scale-Revisited, WAICD = The Worries About ICDs Scale modification of the 26-item Index of Subjective Concerns for People with ICDs (ISCP- ICD), EXPECT ICD = Expectations towards ICD therapy questionnaire, SSQ6 = Social Support Questionnaire (short version), MLHFQ = Minnesota Living with Heart Failure Questionnaire, EQ-5D = EuroQol-5 Dimension, EuroQol-5D-3 = EuroQol-5 Dimension 3 level.

Demographic and Clinical Characteristics

Three papers analysed data from participants enrolled in the Webcare RCT (Habibović, et al., 2017b; Habibović et al., 2018; Pedersen et al., 2018). Four papers used data collected from 3067 participants recruited from the Swedish ICD and Pacemaker Registry (Israelsson et al., 2018; Miller et al., 2016; Thylén et al., 2014; Thylén et al., 2016), and two papers used data collected from 139 ICD-recipients recruited by Wong et al. (2014) (Wong, 2016; Wong, 2019). Adjusting for these papers use of data from the same sample(s), the 19 papers included a total of 5521 ICD-recipients.

The studies were conducted in middle to high income countries. Most papers recruited ICD-recipients from Europe or Asia, with one multicenter study including participants from North America and Oceania (Lee et al., 2020). All papers specified participants' sex, with a total of 4395 out of 5521 (80%) being male. Age of participants ranged from 19 to 94 years. Seventeen papers reported average age with the mean ranging from 58.9 (Habibović, et al., 2017b) to 68 (Varghese et al., 2019). Two papers only reported age in category ranges, with 72% and 86% of the samples being aged 50 and over (Inchikura et al., 2017; Wong, 2016).

Fifteen papers specified participants' ICD-implant indication, with 2321 ICD-recipients receiving their ICD for primary prevention and 2555 for secondary prevention. Four papers did not include ICD indication information, with indication unknown for 645 participants (Farahani et al., 2016; Lee et al., 2020; Wong 2016; Wong, 2018; Wong 2019). Eighteen papers included data on the experience of ICD shock, with 1693 participants reported to have had at least one device shock. One paper (Varghese et al., 2019) reported 27 participants experienced 'phantom shock' which is the sensation of shock in the absence of an objective ICD discharge (Juan & Pollack, 2010).

Most papers reported the prevalence of distress in ICD-recipients. The prevalence of clinically significant symptoms of anxiety and depression (measured via self-report) ranged from 7% to 28% for depression (Amaiz et al., 2017; Rahmawati et al., 2016) and 9% to 20.5% for anxiety (Habibović, et al., 2017b; Miller et al., 2016). Two papers evaluated anxiety and depression with the MINI 'psychiatric interview' and reported 2-4% met criteria for 'new onset depression', 6% met criteria for 'dysthymia' and 1% met criteria for anxiety (Amiaz et al., 2016; Amaiz et al., 2017).

Research Design

Thirteen papers implemented a cross-sectional design. Three papers performed secondary analysis of data collected as part of the Webcare RCT (Habibović et al., 2017b; Habibović et al., 2018; Pedersen et al., 2018). Two papers utilised a longitudinal, repeated measures design of consecutively implanted ICD-recipients (Amiaz et al., 2017; Starrenburg et al., 2014). One paper (Rottmann et al., 2018) conducted secondary analysis of data collected in the MIDAS study, a prospective longitudinal study of consecutively implanted ICD-recipients (Pedersen et al., 2010).

Methodological Quality

The quality ratings of included papers using the CCAT can be found in Appendix 1.6, p.140-141. Fourteen papers scored between 53% and 70% indicating moderate quality. Five papers scored between 45% and 48%, indicating low quality and caution should be applied when interpreting the findings as these studies did not meet several quality assessment criteria.

The main methodological limitations included: not collecting data on or statistically controlling for confounding variables, lack of reporting pre- or post-hoc power calculations, lack of information regarding attrition/missing data, and absence of reporting confidence intervals or effect sizes. The failure of most studies to report data on confounding variables (e.g., history of emotional distress, treatment with psychotropic medication or psychological therapy) means it is unclear whether participants experienced new difficulties or worsening of a pre-existing condition following ICD-implantation. Additionally, most papers implemented cross-sectional designs and therefore causal inferences about the relationship between demographic, clinical, ICD-specific and psychosocial factors and ICD-recipient's emotional distress cannot be drawn.

With regards to ethics, issues included insufficient detail on funding or conflict of interests and information on researchers' relationships with participants.

Findings

Factors influencing anxiety and depression were identified from each study. To synthesise the evidence, the identified factors were divided into four categories: socio-demographic, clinical (cardiac related and co-occurring health conditions), ICD-specific and psychosocial factors (See Figure 2).

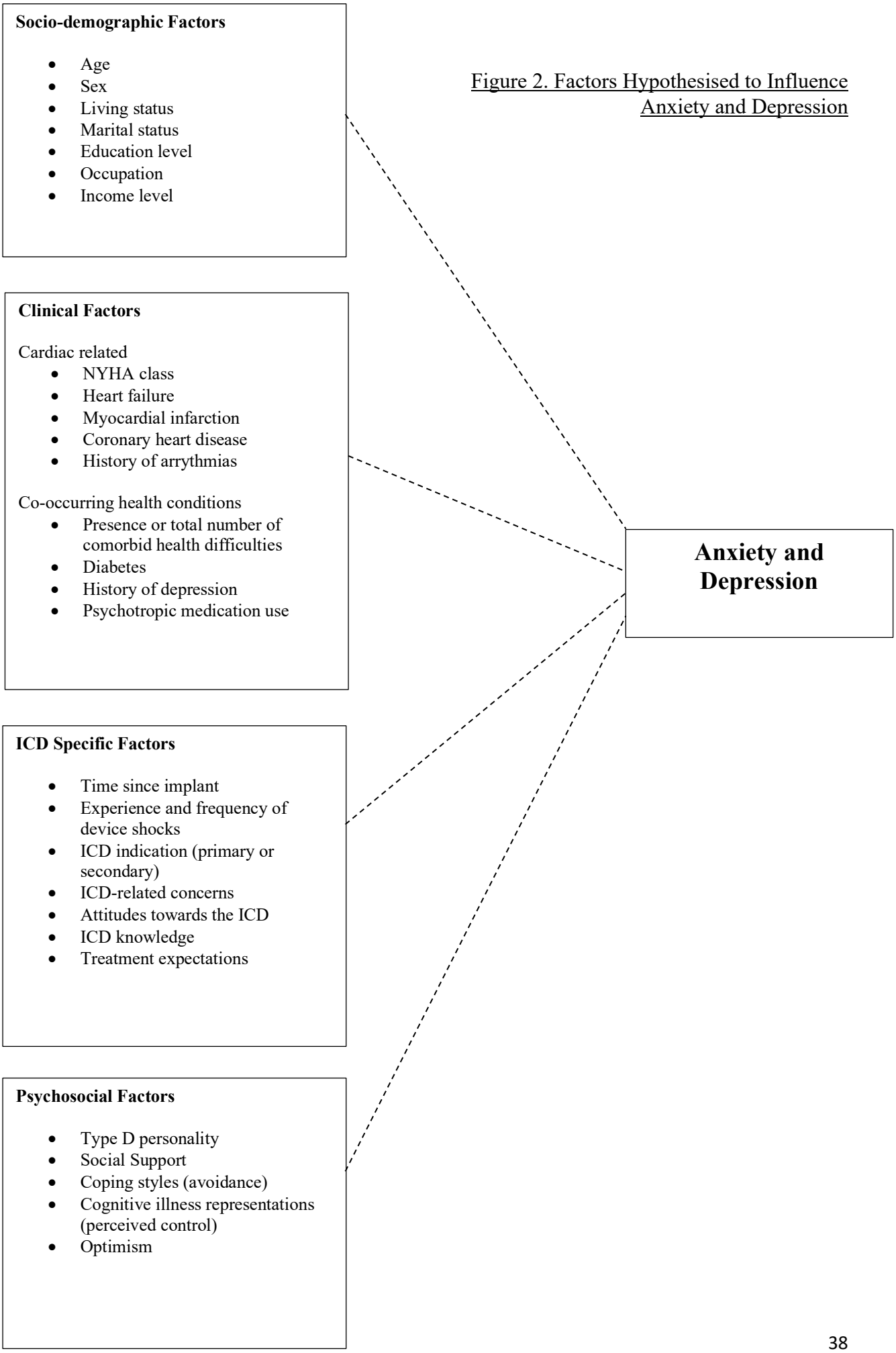

Figure 2. Factors Hypothesised to Influence Anxiety and Depression

Main Findings

Socio-demographic Factors

Age

Ten studies reported on age as a predictive factor for anxiety and depression. Five papers reported no association between age and ICD-recipient's anxiety and depression scores (Farahani et al., 2016; Habibović et al., 2018; Israelsson et al., 2018; Rahmawati et al., 2016; Rottmann et al., 2018). Papers with larger sample sizes, found younger age was associated with anxiety and depression (Habibović et al., 2017b; Thylén et al., 2014), and younger age was independently associated with anxiety in male ICD-recipients (Miller et al., 2016). Two papers found older age (>60) was associated with ICD-recipients depression scores, however, the quality ratings were low, limiting confidence in these findings (Wong, 2016; Wong 2019).

Sex

Twelve studies reported on sex as a predictive factor for emotional distress. Five papers found no association between sex and ICD-recipients' depression and anxiety scores (Amaiz et al., 2016; Habibović et al., 2018; Ichikura et al., 2017; Rottmann et al., 2018; Wong, 2016). Studies recruiting a larger number of female ICD-recipients, found females reported higher anxiety compared to males, after controlling for clinical confounders (Miller et al., 2016; Starrenburg et al., 2014). Consistent with this, three papers reported female sex was correlated with or emerged as an independent predictor of anxiety (Israelsson et al., 2018; Thylén et al., 2014; Wong 2018).

Rahmawati et al. (2016) found female sex was associated with depression not anxiety, while one paper reported male sex was associated with depression (Farahani et al., 2016). The quality of the Farahani et al. (2016) paper was low, therefore reducing confidence in this finding.

Marital & Living status

Of the five papers examining the impact of marital status on anxiety and depression, the studies ranged from moderate to low quality with only the low-quality papers reporting a link between being unmarried and higher risk of depression (Wong, 2016; Wong, 2019).

Three papers reported on living situation as a factor associated with anxiety and depression. Data revealed a significant relationship between living alone and higher anxiety and depression in ICD-recipients (Ichikura et al., 2017; Thylén et al., 2014). Nevertheless, one paper found cohabitation status was not associated with anxiety or depression (Israelsson et al., 2018).

Education, income level and occupational status

Six studies reported on education level as a predictor of anxiety and depression. Three out of four papers, which found no association between education level and participants anxiety and depression were of moderate quality (Farahani et al., 2016; Habibović, et al., 2017b; Habibović, et al., 2018; Israelsson et al., 2018). Nevertheless, two papers ranging from low to moderate quality reported lower education status was associated with depression (Miller et al., 2016; Wong et al., 2019).

Six papers examined income level and occupational status as associating factors for anxiety and depression. Results revealed no significant relationship between income level or employment status and ICD-recipients' anxiety and depression (Amaiz et al., 2016; Farahani et al., 2016; Habibović et al., 2017b; Ichikura et al., 2017). One paper found being unemployed was correlated with ICD-recipient's anxiety scores (Israelsson et al., 2018), while Wong (2019) found being retired was negatively associated with depression.

Clinical Factors

Cardiac-related

Nine papers reported on cardiac related factors including the New York Heart Association (NYHA) classification, presence of heart failure (HF), coronary heart disease (CHD), history of myocardial infarction (MI) and arrythmias.

NYHA is a classification system used to describe the severity of HF symptoms based on how limited patients are during physical activity (Bennet et al., 2002). There are four classes ranging from class I (no limitation of physical activity) to class IV (unable to engage in physical activity without discomfort). Two papers found an association between higher NYHA class and increased depression scores (Amaiz et al., 2016; Amaiz et al., 2017). However, two studies found NYHA class did not predict change in anxiety or depression at 12-month follow-up (Habibović et al., 2018) or independently predict anxiety and depression scores (Rahmawati et al., 2016).

Six studies examined the relationship between history of cardiac-related disease factors and anxiety and depression. Two studies of moderate quality found history of HF and MI was associated with anxiety and depression (Thylén et al., 2014) and 'symptomatic' HF was associated with persistent anxiety at 12-months (Rottmann et al., 2018). One paper of moderate quality found no association between baseline HF diagnosis and trajectories of anxiety over 12-months (Habibović et al., 2017b). Wong (2016) also found no association between history of HF or history of arrhythmias and ICD-recipients' anxiety and depression**.** The quality of this paper was low, limiting confidence in these findings.

Additionally, two low quality papers reported an association between CHD and anxiety and depression in ICD-recipients (Wong, 2016; Wong 2019). Consistent with this, Amaiz et al. (2016) found participants who had undergone a coronary artery bypass graft (a surgical procedure for CHD) reported increased depression. Nevertheless, higher quality evidence is needed before a firm conclusion about the relationship between CHD and risk of distress in ICD-recipients can be drawn.

Co-occurring health conditions

Seven papers reported on the relationship between co-occurring health issues and ICD-recipients' symptoms of anxiety and depression. The results were inconsistent with one study finding no association between Charlson Comorbidity Index (CCI) and ICD-recipients' trajectories of anxiety during 12-month follow-up (Habibović et al., 2017b). However, Habibović et al. (2018) reported higher medical co-morbidity (measured using the CCI) was associated with increased anxiety and depression. Similarly, the presence of comorbidities was correlated with ICD-recipient's anxiety and depression scores (Israelsson et al., 2018). Moreover, Miller et al. (2016) reported the total number of

comorbidities were associated with increased anxiety and depression in male ICD-recipients.

Three papers explored the relationship between diabetes and ICD-recipients' distress (Amaiz et al., 2016; Wong, 2018; Wong 2019). Of the three papers examining the relationship between diabetes and emotional distress, the studies ranged from moderate to low quality with only the low-quality papers finding a link between diabetes and increased depression (Wong, 2018; Wong 2019).

Depression History

Two papers reported personal/family history of emotional distress as a predictive factor for depression. One moderate quality paper found ICD-recipients with a history of mental health difficulties and psychotropic medication use reported higher depression scores during 12-month follow-up (Amaiz et al., 2017). Furthermore, a low-quality paper found an independent association between family history of depression and ICD-recipients depression scores (Farahani et al., 2016).

ICD-specific factors

ICD indication

Six studies reported on ICD indication (primary vs secondary prevention) as a predictive factor for anxiety and depression. Overall, the findings were variable, with three studies finding no association between ICD indication and anxiety or depression (Habibović et al., 2017b; Habibović et al., 2018; Thylén et al., 2014). Conversely, secondary ICD indication emerged as an independent predictor of anxiety and depression in male ICD-

recipients (Miller et al., 2016). Similarly, data from Rottmann et al. (2018) revealed secondary ICD indication was associated with persistent anxiety during 12-month follow-up. Rahmawati et al. (2016) found the opposite trend with primary indication being associated with ICD-recipient's trait anxiety scores.

Time since implant

Nine papers examined the relationship between time since implant and ICD-recipients' emotional distress. Five papers implementing a cross-sectional design found no association between time since implant and ICD-recipients' anxiety or depression scores (Amaiz et al., 2016; Farahani et al., 2016; Israelesson et al., 2018; Thylén et al., 2014; Wong, 2016). Nevertheless, one cross-sectional study reported longer time since implant was associated with higher depression levels in male ICD-recipients (Miller et al., 2016).

Overall, studies implementing longitudinal designs found significant decreases in ICD-recipients' anxiety and depression scores between baseline and 12-month follow-up (Amaiz et al., 2017; Rottmann et al., 2018; Starrenburg et at., 2014). However, Starrenburg et al. (2014) reported a trend in which depression scores reduced at two months post-implant, followed by a return to pre-implant levels at 12-months.

Device Shocks

Fourteen papers reported on the experience of device shock as a predictive factor for anxiety and depression. Data was inconsistent, with seven studies reporting no association between experience/frequency of device shocks and ICD-recipients distress (Amaiz et al., 2017; Habibovic et al., 2017b; Ichikura et al., 2017; Israelesson et al 2018; Rahmawati et al., 2016; Thylén et al., 2014; Wong 2016).

Conversely, two papers of moderate quality, found device shock independently predicted anxiety in male ICD-recipients (Miller et al., 2016) and was associated with persistent anxiety during 12-month follow-up (Rottmann et al., 2018). Data also showed a significant relationship between device shock and ICD-recipients' depression scores (Farahani et al., 2016) and 'phantom shocks' were associated with increased anxiety (Varghese et al., 2019). Nevertheless, the quality of these papers was low, limiting the confidence in these findings.

Moderate quality papers found device shocks were no longer associated with depression in ICD-recipients after controlling for NYHA class and HF diagnosis (Amaiz et al., 2016). Similarly, there was no direct effect of device shock on ICD-recipients' anxiety and depression after controlling for ICD-related concerns, ICD knowledge and time since implant (Lee et al., 2020; Thylén et al., 2016).

ICD-related concerns

Four moderate quality papers explored the influence of ICD-related concerns on emotional distress. The findings were consistent with all four papers finding a significant association between elevated ICD-related concerns and increased anxiety and depression (Israelsson et al., 2018; Lee et al., 2020; Thylén et al., 2014; Thylén et al., 2016). Moreover, elevated ICD-related concerns emerged as the strongest predictor of probability of anxiety and depression symptoms, with odds ratios of 4.224 and 2.919 respectively (Thylén et al., 2014). Additionally, data indicated elevated ICD-related concerns statistically mediated the relationship between device shock and anxiety and depression (Lee et al., 2020; Thylén., 2016).

Attitudes/ knowledge of the ICD

Three studies with moderate quality ratings, explored the relationship between other ICD-related factors and emotional distress. One paper found ICD-recipients' attitudes towards their device were positively associated with depression (Amaiz et al., 2016). Results also revealed perceptions of worse ICD experience, low ICD knowledge and negative treatment expectations were associated with anxiety or depression (Miller et al., 2016; Pedersen et al., 2018). However, Pedersen et al. (2018) noted negative treatment expectations were weakly associated with depression at 12-months after controlling for Type D personality.

Psychosocial Factors

Personality

Five papers reported on personality type as a predictive factor for distress. Overall, four papers, with moderate quality ratings found Type D personality was associated with ICD-recipients' anxiety and depression scores during follow-up (Habibović, et al., 2017b; Habibović, et al., 2018; Israelsson et al., 2018; Miller et al., 2016). Nevertheless, Type D personality did not independently predict anxiety and depression after controlling for sex, device shocks and comorbid HF (Pedersen et al., 2018).

Social Support

Two moderate quality papers reported on perceived social support as a predictive factor for anxiety and depression. One paper examining sex differences, found perceptions of social support predicted depression in male and female ICD-recipients (Miller et al., 2016). Rottmann et al. (2018) also found higher ratings of social support were associated with reduced anxiety and depression during 12-month follow-up.

Coping Styles

One paper reported on coping styles including avoidance behaviours as a factor related to depression in ICD-recipients. Data indicated avoidance behaviours (e.g., avoidance of activity or places) were associated with heightened odds of depressive symptoms (Ichikura et al., 2017). The quality of this paper was moderate, however, the cause-and-effect relationship between avoidance and depression is unclear due to the implementation of a cross-sectional design.

Illness Representations

Three papers with moderate quality ratings reported on the relationship between illness representations and emotional distress. Results showed significant associations between low perceptions of control and higher anxiety and depression scores in ICD-recipients (Israelsson et al., 2018; Lee et al., 2020; Miller et al., 2016).

Optimism

One moderate quality paper reported on positive psychological constructs as a predictive factor for anxiety and depression. Results showed baseline optimism was negatively associated with ICD-recipient's anxiety and depression at 12-month follow-up, after controlling for clinical, demographic and personality variables (Habibović et al., 2018). Baseline optimism was no longer associated with change in anxiety and depression after controlling for baseline distress. The paper also suffered from limitations including excluding a high number of participants due to incomplete measures.

Discussion

The aim of this review was to systematically review the factors influencing anxiety and depression in ICD-recipients. A summary of the main findings will be presented in the context of the reviewed papers methodological quality. Similar to a previous systematic review investigating distress in ICD-recipients (Magyar et al., 2011) the reviewed studies reported a large range in the prevalence of self-reported clinically significant symptoms of anxiety (9% to 25%) and depression (7% to 28%). The variation in prevalence rates may be explained by inter-study differences in time between ICD-implant and study commencement, study design, and differences in measures or clinical threshold criteria employed.

Socio-demographic factors

There is moderate quality evidence to suggest that younger age is associated with increased anxiety and depression in ICD-recipients (Habibović et al., 2017b; Miller et al., 2016; Thylén et al., 2014). This finding is consistent with a previous review reporting younger age (<50) was associated with poorer adjustment in ICD-recipients (Kajanová et al., 2014).

Results provided tentative evidence that female sex was associated with increased anxiety in ICD-recipients (Israelsson et al., 2018; Miller et al., 2016; Starrenburg et al., 2014; Thylén et al., 2014). These findings are consistent with a review which reported greater anxiety among female ICD-recipients (Freedenberg et al., 2011). Nevertheless, this result may reflect the well-documented finding, that the prevalence rate for anxiety in the general population is higher in females (Kessler et al., 1994). Additionally, some studies found no relationship between female sex and anxiety (Amaiz et al., 2016;

Habibović et al., 2018; Ichikura et al., 2017; Rottmann et al., 2018; Wong, 2016). However, these findings should be interpreted with caution as the papers did not report power calculations and recruited a small sample of female ICD-recipients ($N < 60$). Consequently, these papers may not have been adequately powered to identify sex differences.

Overall, evidence indicated no significant association between marital status, education level income level or employment status and anxiety and depression ICD-recipients (Amaiz et al., 2016; Farahani et al., 2016; Habibović et al., 2017b; Habibović et al., 2018; Ichikura et al., 2017; Israelsson et al., 2018). There was some moderate quality evidence to suggest a significant relationship between living alone and increased risk of distress in ICD-recipients (Ichikura et al., 2017; Thylén et al., 2014).

Clinical factors

Results provided tentative evidence that higher NYHA class, HF or CHD were associated with increased anxiety and or depression in ICD-recipients (Amaiz et al., 2016; Amaiz et al., 2017; Rottmann et al., 2018; Thylén et al., 2014; Wong 2016; Wong, 2019). These findings support, previous research reporting a significant relationship between symptomatic HF and distress in ICD-recipients (Freedenberg et al., 2011). Nevertheless, some papers found no relationship between NYHA class and history of HF and emotional distress (Habibović et al., 2017b; Habibović et al., 2018; Rahmawati et al., 2016; Wong, 2016). The mixed results may be partially explained by inter-study variance in the clinical characteristics of participants. The papers finding no association between NYHA class or HF diagnosis and distress recruited a higher proportion of ICD-recipients within

NYHA classification I and II, suggesting milder severity of HF (Habibović et al., 2018; Rahmawati et al., 2016).

Results provided preliminary evidence that the presence of or total number of co-morbidities are associated with anxiety and depression in ICD-recipients (Habibović et al., 2018; Israelson et al., 2018; Miller et al., 2016; Wong, 2018). Nevertheless, one paper found no association between Charlson Comorbidity Index and ICD-recipients' trajectories of anxiety at 12-months (Habibović et al., 2017b). There was significant variance in how data on co-occurring conditions were measured including self-report (Israelsson et al., 2018), review of medical notes (Amaiz et al., 2016) or a validated tool (the CCI) (e.g., Habibović et al., 2017b). Future research using a standardised approach to measuring comorbidities, that avoids methods prone to recall bias (i.e., self-report) are required to fully understand the influence comorbidities have on ICD-recipients' emotional distress over time.

There was low to moderate quality evidence to suggest ICD-recipients with a personal or family history of mental health difficulties, and psychotropic medication use were at greater risk of depression (Amaiz et al., 2017; Farhani et al., 2016). Future research is required to identify if these factors are associated with increased risk of anxiety in ICD-recipients.

ICD-specific factors

Collectively results showed the relationship between device shock and distress is not straightforward. Evidence was inconsistent with seven out of fourteen papers finding no association between device shock and ICD-recipients' anxiety and depression. This

finding is similar to results of a systematic review reporting only 10 out of 29 studies found a relationship between device shock and distress (Manzoni et al., 2015).

There was preliminary evidence to suggest device shock does not have a direct effect on ICD-recipients' distress. Device shock had no effect on ICD-recipient's anxiety and depression after controlling for NYHA class and ICD-related concerns (Amaiz et al., 2016; Thylén et al., 2016). Instead, evidence suggested the relationship between shock and emotional distress was statistically mediated by elevated ICD-related concerns and perceptions of control (Lee et al., 2020; Thylén et al., 2016).

There was heterogeneity in how data on ICD shock experience was collected, with several papers collecting data via self-report (Lee et al., 2020; Thylén et al., 2016) while other studies gathered objective data from device interrogation (Rottmann et al., 2018). It is possible the studies collecting shock data via self-report were prone to recall bias, which may affect the findings. Data has shown, 29% of ICD-recipients underestimated the number of shocks received, and longer duration of implant was associated with increased inaccuracy (Ahmad et al., 2000).

Longitudinal studies found reductions in ICD-recipients' anxiety or depression scores between baseline (pre-implant) and 12-month follow-up (Amaiz et al., 2017; Rottmann et al., 2018; Starrenburg et at., 2014). However, the cross-sectional studies found no relationship between time since implant and ICD-recipients anxiety and depression (Amaiz et al., 2016; Farahani et al., 2016; Israelesson et al., 2018; Thylén 2014; Wong, 2016).

These findings suggest the choice of research design can influence whether an effect of time on ICD-recipients distress is detected. For cross-sectional studies, there was inter-study variance in the time elapsed between ICD-implant and study commencement, making it difficult to make comparisons between studies. The longitudinal studies investigating the impact of time also had limitations. Two papers did not collect data on confounding factors including history of distress or treatment with medication or therapy (Rottmann et al., 2018; Starrenburg et at., 2014). Accordingly, further studies using prospective and longitudinal designs, with controls for confounding factors are required to accurately describe the trajectories of anxiety and depression in ICD-recipients over time.

There is moderate quality evidence to suggest a significant relationship between ICD-related concerns and ICD-recipients' anxiety and depression (Israelsson et al., 2018; Lee et al., 2020; Thylén et al., 2014; Thylén et al., 2016). Data also showed elevated ICD related concerns mediated the relationship between device shock and emotional distress (Lee et al., 2020; Thylén et al., 2016). These findings are consistent with earlier research which reported ICD-related concerns emerged as an independent determinant of distress after controlling for number of device shocks received (Pedersen et al., 2005).

Nevertheless, the results should be interpreted with caution due to studies use of cross-sectional designs, which means no conclusions about the causal relationship between ICD-related concerns, device shock and distress can be drawn. Future research using prospective longitudinal designs is required to replicate the findings and further elucidate the relationship between anxiety, depression, ICD-related concerns and device shock.

Evidence also revealed a significant independent association between ICD-specific factors including perceptions of worse ICD experience, low ICD knowledge and negative treatment expectations and anxiety or depression (Miller et al., 2016; Pedersen et al., 2018). This finding supports previous research indicating inappropriate patient education/knowledge was associated with distress in ICD-recipients (Kajanová et al., 2014).

Psychosocial factors

Evidence suggested psychosocial factors including coping styles (avoidance) and cognitive illness representations (low perceptions of control) were associated with increased anxiety and or depression in ICD-recipients (Ichikura et al., 2017; Israelsson et al., 2018; Lee et al., 2020; Miller et al., 2020). These findings are consistent with the self-regulation model (Leventhal et al.,1980) which highlights the role cognitive illness representations play in the emotional adjustment to health conditions. Nevertheless, these findings should be interpreted with caution as these papers suffered methodological limitations. The papers did not adequately control for extraneous factors (e.g., history of anxiety or depression or psychotropic medication use) and implemented cross-sectional designs, which precludes conclusions about causality. Accordingly, subsequent longitudinal studies controlling for confounding variables are required to identify whether perceptions of control and avoidance behaviours predict emotional adjustment in ICD-recipients over time.

There was tentative evidence to suggest lower perceptions of social support was associated with depression (Miller et al., 2016) and high ratings associated with

improvement in anxiety and depression in ICD-recipients (Rottmann et al., 2018). Nevertheless, the papers acknowledged methodological limitations including not collecting data on actual social support received post ICD-implantation. Perceptions of social support can be viewed as an index of intrapersonal processes, shaped by relational schemas as opposed to providing a measure of actual environmental supports (Uchino, 2009). Consequently, future studies could examine the influence that actual received support and perceptions of social support have on the emotional adjustment of ICD-recipients to elucidate targets for intervention.

Overall, data suggested Type D personality was associated with increased anxiety and depression in ICD-recipients (Habibović, et al., 2017b; Habibović, et al., 2018; Israelsson et al., 2018; Miller et al., 2016). This finding is consistent with a previous review indicating Type D personality is linked to distress in ICD-recipients (Kajanová et al., 2014). Nevertheless, Type D personality did not predict distress after controlling for device shock, sex and co-occurring HF (Pedersen et al., 2018).

Further research, controlling for confounding factors is required to identify whether Type D personality is an independent predictor of distress in ICD-recipients or overlaps with other constructs. There has been debate in the literature about the validity and utility of the Type D personality construct because the increased negative affectivity component (central to the construct) overlaps with symptoms of depression (Stepto & Molloy, 2007).

Finally, there was preliminary evidence to suggest after controlling for demographic, clinical and personality variables, baseline optimism was associated with reduced anxiety

and depression in ICD-recipients (Habibović, et al., 2018). This finding should be interpreted with caution as the study had limitations including a significant number of participants being excluded from the analysis. Consequently, the sample could be biased towards ICD-recipients who are motivated to participate or experience less severe health impacts, which may affect the generalisability of the findings.

Methodological Limitations

The current review suffered from methodological limitations and the results should be interpreted with caution. First, 80% of ICD-recipients in included studies were male. This reflects the ICD population with females not receiving ICD implants at the same rates as their male counterparts (McSweeney et al., 2012). It therefore remains unclear if the findings can be generalised to female ICD-recipients.

Second, most studies did not collect data on ICD-recipients' history of distress. It is therefore unknown if participants anxiety and depression symptoms existed prior to ICD-implantation or developed in response to implantation.

Third, included papers were conducted in middle-to-high income countries and most studies took place in Europe or Asia. There are documented differences between high income and developing countries in terms of access to ICD treatment (Sani & Mayosi, 2017). Therefore, it will be useful to include research from developing countries to increase the cultural validity and generalisability of the findings.

Most papers relied on self-report measures of emotional distress, while only two papers supplemented data with 'diagnostic interviews' (Amaiz et al., 2016; Amaiz et al., 2017). The use of self-report measures of distress is subject to sources of bias including social-desirability bias and regression to the mean, which may impact the findings.

Additionally, only two of the included studies reported a power calculation (Farhani et al., 2016; Ichikura et al., 2017) to justify the recruited sample size. Consequently, precluding the risk of occurrence of type II error in the other studies is challenging because it is unclear whether studies were adequately powered to investigate the relationship between multiple variables. Nevertheless, findings, particularly in relation to psychosocial variables and ICD-related factors were replicated across studies, giving a provisional indication this risk was not high.

Conclusion

Overall, this review identified socio-demographic factors (female sex, younger age, living alone), clinical factors (HF, history of CHD or emotional distress), ICD-specific factors (elevated ICD-related concerns, low ICD knowledge, negative treatment expectations), and psychosocial factors (avoidance behaviours, low perceived control, and Type D personality) may worsen anxiety and depression in ICD-recipients. But the generally poor methodological quality of papers suggests these results should be treated cautiously. Future research that is: adequately powered, employs prospective longitudinal designs and controls for confounding factors is required to fully understand the relationship between sociodemographic, clinical, ICD-specific and psychosocial factors and distress in ICD-recipients over time.

Relevance to Clinical Practice

The findings from this review support earlier research (Pedersen et al., 2005) demonstrating a relationship between elevated ICD-related concerns and emotional distress. Accordingly, routine screening for ICD-related concerns using the validated ICDC questionnaire may help identify patients at risk of developing anxiety and depression post ICD-implant.

The results provide preliminary evidence to suggest ICD-recipients with symptomatic HF or CHD, female ICD-recipients, those with Type D personality, younger ICD-recipients (<50), and those with a history of distress or previous treatment with psychotropic medication may be at increased risk of distress. Therefore, these characteristics may be useful in identifying those at risk for distress after implant.

Results also provide initial evidence to suggest knowledge of the ICD, coping styles (avoidance), cognitive appraisals (ICD-related concerns, treatment expectations and perceptions of control) influence anxiety and depression in ICD-recipients. These factors are modifiable and may represent useful factors to target during educational or psychosocial interventions. Results also suggest perceptions of social support are associated with emotional outcomes in ICD-recipients. Therefore, relational interventions aimed at improving ICD-recipients' access to social support or ability to utilise their social networks may be useful.

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Chapter Two: Major Research Project

Trajectories of Anxiety and Depression in Patients with Chronic Heart Failure

Prepared in accordance with the author requirements for submission to the Journal of Clinical Nursing (Appendix 1.1, p.126)

Plain Language Summary

Background: Research suggests people with chronic heart failure (CHF) report increased rates of anxiety and depression compared to the general population. CHF patients with anxiety and depression are at increased risk of poorer outcomes including hospital readmission. There has been little research looking at how anxiety and depression develops over time in people with CHF. It is important to explore how anxiety and depression develops to find out whether anxiety or depression symptoms are short-lived or persistent.

Aim: To describe how symptoms of anxiety and depression develop over 12-months in a sample of people with CHF.

Methods: The project involved analysing data collected from a previous study which looked at the palliative care needs of CHF patients (Campbell et al., 2018). Data were analysed using statistical tests. Ethical approval for this project was granted by NHS Greater Glasgow and Clyde's Research and Innovation department.

Results: Overall, the proportion of the sample reporting anxiety and depression symptoms was higher during a period of hospital admission and reduced significantly by 12-months. Data also indicated the majority of the sample did not report anxiety or depression or experienced resolution in their symptoms at 4, 8 and 12-month follow-up. Nevertheless, results showed 21% of the sample who reported symptoms of anxiety and depression during hospital admission experienced persistent symptoms at 12-month follow-up. Furthermore, a small percentage of patients who were anxiety or depression

symptom free during hospital admission went on to develop anxiety or depression by 12-months.

Conclusions and implications: Although the majority of people with CHF in this sample experienced no or relatively short-lived symptoms of anxiety and depression, some experienced persistent symptoms. Routine and repeated screening for anxiety and depression in outpatient settings or primary care is recommended for this population.

References: Campbell, R. T., Petrie, M. C., Jackson, C. E., Jhund, P. S., Wright, A., Gardner, R. S., ... & McMurray, J. J. (2018). Which patients with heart failure should receive specialist palliative care? *European journal of heart failure*, *20*(9), 1338-1347.

Abstract

Aims and Objectives: To describe the trajectory of anxiety and depression in Chronic Heart Failure (CHF) patients during 12-month follow-up and to identify characteristics independently associated with anxiety and depression.

Background: CHF patients with depression and anxiety are at increased risk of poorer outcomes including hospital readmission. There is limited research describing the trajectories of anxiety and depression in CHF patients over time.

Design: The study was a secondary analysis of data collected in a longitudinal study investigating the palliative care needs of 272 CHF patients in Glasgow.

Methods: Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS) at baseline and every four-months.

Results: From baseline to 12-months, there was a significant reduction in the proportion of CHF patients reporting symptoms of anxiety (43.5% vs 25%) and depression (40% vs 27.4%). Looking at change in HADS scores over 12-months, 54.3% of patients were free of significant anxiety at all assessments, 21.7% showed an improvement in initially distressing anxiety, and 2.2% developed anxiety as the study progressed. Based on change in HADS depression scores across 12-months, 53.7% did not report significant depression, 18.9% experienced resolution of depression symptoms, and 6.3% went on to develop depression as the study progressed. One in five patients experienced persistent anxiety and depression throughout. In regression analysis, baseline anxiety, health-related quality of life, history of depression and female sex emerged as predictors of

anxiety, while baseline depression, history of depression, antidepressant medication use, and female sex predicted depression.

Conclusions: Results suggest a significant reduction in the proportion of CHF patients reporting clinically significant anxiety and depression from baseline to 12-month follow-up. Although there was a subset of participants that experienced persistent symptoms of anxiety and depression.

Relevance to Clinical Practice: Routine screening for anxiety and depression in CHF patients is recommended.

Keywords: anxiety, depression, heart failure.

Introduction

Chronic Heart failure (CHF) is associated with poor prognosis in terms of mortality and on-going symptom burden (Soriano et al., 2010). The disease course of CHF is characterised by phases of stability, punctuated by periods of acute worsening of symptoms, with these exacerbations often being unexpected and life threatening (Goodlin, 2009).

Accordingly, psychological adjustment to CHF is challenging. The prevalence of depression is about one in five, with estimates influenced by the use of diagnostic interview versus self-report methods (19.3% and 33.6% respectively) (Rutledge, Reis, Linke, Greenberg & Mills, 2006). Additionally, a systematic review and meta-analysis reported a pool prevalence of 13.1% for 'anxiety disorders' in people with CHF, and 30% self-reported clinically significant anxiety symptoms (Easton, Coventry, Lovell, Carter & Deaton, 2016). This is higher than the point prevalence estimates for the general population of 12.9% for depression and 7.2% for anxiety (Lim et al., 2018; Martín-Merino, Ruigómez, Wallander, Johansson & García-Rodríguez, 2010).

CHF patients who experience anxiety and depression have poorer outcomes compared to their non-distressed counterparts. Evidence suggests depression is associated with increased risk of both death and hospital readmission plus poorer health-related quality of life (HR-QoL) (Dekker et al., 2011; Rutledge et al., 2006). Anxiety has been linked to HF-related hospital readmission and poorer functioning (Shen et al., 2011; Tsuchihashi-Makaya, Kato, Chishaki, Takeshita & Tsutsui, 2009).

Psychological theory can be applied to understand emotional adjustment to CHF. The working model of adjustment asserts critical events (development of initial symptoms of illness, diagnosis, and disease progression) initially disrupts an individual's 'emotional equilibrium' leading to distress (Moss-Morris, 2013). In accordance with this, data indicates the development of depression is associated with periods of acute worsening of CHF symptoms (Johansson et al., 2013), and people hospitalised with CHF report higher rates of depression compared to outpatients experiencing stability in their symptoms (Konstam, Moser & De Jong, 2005).

The working model of adjustment also proposes background factors (e.g., social support, age, previous life experiences), on-going illness-specific factors (e.g., the nature of symptoms, degree of uncertainty) and cognitive-behavioural factors (e.g., negative illness representations, avoidant coping) can lead to on-going emotional disequilibrium/adjustment difficulties (Moss-Morris, 2013). Research in CHF populations appears to support these predictions. Depression in CHF patients is associated with demographic factors (female sex), social factors (quality of social support), clinical factors (functional severity of CHF as measured by New York Heart Association Functional Classification – NYHA class), and psychological factors (coping styles, low perceptions of control) (Haworth et al., 2005; Lerdal, Hofoss, Gay & Fagermoen, 2019; Tsuchihashi-Makaya et al., 2009).

Comparatively fewer studies have examined predictors of anxiety in CHF patients and most research is cross-sectional. From these studies, increased somatic symptoms, smoking and drinking status, reduced HR-QoL and history of depression have all been associated with anxiety in cardiac populations (Allabadi et al., 2019; Årestedt et al.,

2014). Additionally, presence of depression and younger age independently predicted anxiety in sample of outpatients with CHF, while ethnicity, and NYHA class did not (Årestedt et al., 2014).

Trajectories Over Time

There has been limited research investigating the longitudinal trajectories of depression and anxiety in CHF patients (Decker et al., 2011; Johansson et al., 2013; Koenig, Vandermeer, Chambers, Burr-Crutchfield & Johnson, 2006). A study of 256 CHF patients in the US found 15% experienced resolution of 'depressive symptoms' after 3-6 months (Dekker et al., 2011), while a separate study reported 61% had recovered by 18 months (Johansson et al., 2013).

However, not all patients follow an improvement trajectory. Across studies, of the CHF patients who reported clinically significant depression at baseline: at 6 weeks follow-up 27.3% experienced persistent symptoms (Koenig et al., 2006), at 3-6 months 15% experienced persistent depression (Dekker et al., 2011), and at 18-month follow-up and 39% reported persistent depression (Johansson et al., 2013). Additionally, data showed 6% of CHF patients sampled developed clinically significant depression at 3–6-month follow-up (Dekker et al., 2011), and 18% developed depression after 18-months (Johansson et al., 2013).

Patient characteristics including co-occurring health problems, history of emotional distress and psychotropic medication use may predict whether CHF patients follow a 'depression not improved' trajectory at follow-up (Koenig et al., 2006). The

development of depression at follow-up has also been associated with behavioural factors (excess alcohol use), socio-demographic factors (living alone) and baseline disease specific HR-QoL (as measured by the Kansas City Cardiomyopathy Questionnaire - KCCQ) (Havranek, Spertus, Masoudi, Johnes & Rumsfeld, 2004). Surprisingly, depression at follow-up was not associated with indicators of disease severity (NYHA class, ejection fraction %) or commonly identified risk factors for depression in the general population including age (Havranek et al., 2004).

Justification for the Proposed Study

Very few studies examine the trajectories of anxiety in individuals with CHF. Most research is limited by a focus on depression (Volz et al., 2011) and so it is unclear how anxiety symptoms in people with CHF develops over time. The demographic, clinical or psychosocial predictors of anxiety and depression across time in people with CHF also warrant attention.

It is important to explore how anxiety and depression in CHF patients develops to identify whether anxiety and depression are transient or whether difficulties follow a more persistent course. Such information may help to inform clinician's about when to screen for anxiety and depression symptoms (Johansson et al., 2013). Additionally, identifying the demographic and clinical characteristics associated with anxiety and depression is important to help clinicians to identify CHF patients at risk of less favourable outcomes.

Aims

The primary aim of this study was to describe the trajectories of anxiety and depression in a sample of patients with CHF over 12-month follow-up. The secondary aim was to identify baseline demographic and clinical factors that are independently associated with anxiety and depression.

Based on previous research and on the predictions of Moss-Morris's (2013) working model of psychological adjustment it was hypothesised that:

- Levels of anxiety and depression in CHF patients would decrease from baseline (index admission) to 12-month follow-up.
- Anxiety and depressive symptoms would be associated with relevant background factors (e.g., sex, age, history of depression and or anti-depressant use).
- Anxiety and depressive symptoms would be associated with illness-specific factors (e.g., level of symptom burden, disease-specific HR-QoL).
- Anxiety and depressive symptoms would be associated with behavioural factors (e.g., excess alcohol use).

Method

Design

The study was a secondary analysis of longitudinal data which had investigated palliative care needs of people with CHF (Campbell et al., 2018). The design and rationale of the original study has been published elsewhere (Campbell et al., 2015) and included a near consecutively recruited sample of 272 CHF patients who were admitted to hospital and followed up for up to 28-months. 120 (44.1%) of participants had been diagnosed with CHF prior to the index admission and 152 (55.9%) were diagnosed during admission. Eligible participants were aged 18 years and over and met the following inclusion criteria (See table 2).

Table 2 Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Admitted to the Western Infirmary hospital in Glasgow (between 9th January 2013 to 1st December 2014) with a primary diagnosis of acute decompensated HF	• Had a BNP level <100 pg/mL • Lack of capacity to provide informed consent (presented with dementia, learning difficulties, were moribund or unable to read/write in English)
• Fulfilled the European Society of Cardiology (ESC) echocardiographic diagnostic criteria for guidelines for the diagnosis of HF	• Were re-admitted after the index admission (baseline) • Presented with acute coronary syndrome complicated by pulmonary oedema or isolated cor pulmonale
• Had B-type natriuretic peptide (BNP) level > 100 pg/mL • Participants with valvular HF, HF with reduced ejection fraction, and HF with preserved ejection fraction were included	

Ethical Approval

Ethical approval for Campbell and colleagues (2018) study was granted by the West of Scotland Research Ethics committee (REC Ref: 12/WS/0224; IRAS Ref 100839). All enrolled participants consented to 'passive follow-up' through medical record linkage, accessed through the Greater Glasgow and Clyde SafeHaven service. Participants provided consent for their anonymised data being analysed in future research. For the present study, Research and Innovation Management (R&I) approval was obtained from Greater Glasgow & Clyde (See appendix 2.4, p.164-165).

Protocol

Participant's symptom burden, anxiety, depression and HR-QoL (using the patient reported outcome measures detailed below) were assessed during the index admission (baseline), and then at 4-monthly intervals for up to 28-months. Measures were completed during study visits, which took place in the Western Infirmary or in participants own homes, if they were too unwell to travel.

Measures

Demographic, Clinical and Behavioural Data

Baseline demographic, clinical and behavioural characteristics were collected during participants index admission via medial note review and patient interview (Campbell et al., 2015). Demographic information included age (in years), sex (female, male) and ethnicity (Arab/Middle East, Black, South Asian, White). Clinical information included ejection fraction (< 50%, > = 50%), NYHA class (I to IV), HF symptoms (orthopnea, ankle swelling etc.), prior diagnosis of HF (Y/N), history of myocardial infarction (Y/N), atrial fibrillation (Y/N), arrythmia (Y/N), history of other conditions (e.g., diabetes)

(Y/N), history and or current depression (Y/N) and anti-depressant use (Y/N). Data on behavioural factors included smoking status (current smoker, never smoked, ex-smoker) and alcohol use (none, excess, previous excess, within the recommended limits).

Anxiety and Depression

Symptoms of anxiety and depression were assessed with the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983). The HADS contains 14-items, 7 of which measure depression (HADS-D), and 7 measuring anxiety (HADS-A). Items are scored on a 4-point Likert scale. Scores range from 0 to 3, with a total score of 0–21 for each subscale. The authors suggest employing a cut-point of ≥ 8 for each of the constituent subscales, to indicate probable caseness. This cut-off provides sensitivity and specificity of 0.80 (Bjelland, Dahl, Haug & Necklemann, 2002). The Cronbach's alpha values are 0.83 and 0.82 for the HADS-A and HADS-D respectively, indicating the HADS is reliable. The HADS is validated for use in CHF populations (Haworth et al., 2007).

HR-QoL

Perceived HR-QoL was assessed using a HF specific measure, the KCCQ (Kansas City Cardiomyopathy Questionnaire). The KCCQ contains 23-items which aims to quantify: QoL, physical limitations, social limitations, self-efficacy, symptom frequency, symptom burden, and symptom stability (Green, Porter, Bresnahan & Spertus, 2000). The scale comprises of five subscales, and all besides the self-efficacy subscale, can be used to compute an overall summary score. Scores for each subscale range from 0 to 100 with lower scores indicating worse disease-specific HR-QoL. Research has shown the KCCQ

to have good psychometric properties, with one study reporting a Cronbach's alpha of 0.92 (Creber, Polomano, Farrar & Riegel, 2012).

Symptom Burden

Symptom burden was measured with the Edmonton Symptom Assessment Scale (ESAS) (Bruera, Kuehn, Miller, Selmeser & Macmillian, 1991). The ESAS assesses nine symptom areas and their severity: pain, tiredness, drowsiness, lack of appetite, nausea, shortness of breath, fatigue, anxiety, depression and the patient's overall perception of their well-being. The ESAS contains 10 items, where respondents select a score between 0 (no symptom) and 10 (represents the worst). A total score can be calculated ranging from 0 to 100, with higher scores indicating increased symptom burden. The ESAS was developed and validated for use with people living with cancer (Kaasa & Wessel, 2001). Nevertheless, the ESAS has been used in a study of patients with HF and the authors concluded the use of the ESAS alongside the KCCQ provided comprehensive quantitative information on patients physical and emotional distress (Opasich et al., 2008). In the current study, the Cronbach alpha coefficient was .90.

Statistical Analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS, version 26). All tests conducted were two-tailed and an alpha value of ≤.05 indicated statistical significance. Data were presented as Median (*Md*) and Interquartile Range (IQR) for non-normally distributed continuous variables and frequencies and percentages for categorical variables.

The characteristics of participants who completed and did not complete primary outcome measures (PROMs) at baseline were compared. Continuous and normally distributed variables were analysed using the independent t-test while non-normally distributed data were analysed using the Mann-Whitney U test. Differences on categorical variables were analysed using χ^2 (Chi-Square Test of Independence) or Fishers Exact test where the assumptions of Chi-Square were not met.

Longitudinal studies are prone to missing data. Missing data was explored using the missing values analysis feature in SPSS (version 26). For the HADS, there was substantial missing data across follow-up waves. Additionally, Little's missing at completely random test was significant, indicating the data were not missing completely at random.

Consequently, it was decided that the use of multiple imputation methods would not be appropriate and instead analysis used observed data (i.e., listwise deletion). This approach is in accordance with guidance relating to the handling of missing data (Jakobsen, Gluud, Wetterslev & Winkel, 2017). For analysis describing the trajectory of anxiety and depression across follow-up, participants with four complete measurements

of anxiety and depression were included. For regression analysis, participants with at least two complete assessments of anxiety and depression were included in the analysis.

Guidance stipulates that when listwise deletion methods are used to handle missing data, the extent of missing data should be reported on (Jakobsen et al.., 2017). See Figure 3 for the details of participant flow through the study. Additionally, the differences between participants providing one, two, three or four complete measures of anxiety and depression were examined using the χ^2 (Chi-Square Test of Independence) or Fishers Exact test for nominal variables. For continuous variables, differences were examined using one-way ANOVA for normally distributed variables or the Kruskal-Wallis Test for non-normally distributed variables.

Measures of central tendency and dispersion were computed to describe the key outcome variables (participants anxiety and depression scores) over time (baseline, 4, 8 & 12-month follow-up). Additionally, the proportion of participants who reported clinically significant symptoms of anxiety and depression was calculated at Time 1 (baseline), Time 2 (4-months), Time 3 (8-months) and Time 4 (12-months). The standard HADS cut off point of ≥8 was used to categorise participants as having clinically significant anxiety and depression symptoms.

Similar to previous research (Dekker et al., 2011) participants were then assigned to one of four anxiety and depression 'symptom status' groups based on the change or lack of change in their HADS-A and HADS-D scores from baseline to 4, 8 and 12 months (See Table 3). The four groups were: 1) anxiety or depression symptom-free, 2) symptoms improved, 3) symptoms developed, 4) and persistent symptoms.

Table 3 Anxiety and Depression Symptom Status Group Assignment Based on HADS-A and HADS-D Scores at Baseline, 4-, 8- and 12-Month Follow-up

HADS score at baseline	**HADS at 4, 8, 12 months**
0-7	0-7 = Anxiety or depression symptom free
≥8	0-7 = Anxiety or depression symptoms improved
0-7	≥8 = Anxiety or depression symptoms developed
≥8	≥8 = Persistent anxiety or depression symptoms

The Friedman test was used to investigate overall change in participants depression and anxiety scores due to non-normal distribution. Post-hoc testing involved conducting individual Wilcoxon Signed Rank Tests (using Bonferroni adjusted alpha value) to control for Type 1 errors.

Related samples Cochran's Q tests were used to examine if there were significant changes in the proportion of participants reporting clinically significant anxiety and depression symptoms over time (baseline, 4, 8 & 12-month follow-up). The individual alpha level was adjusted using the Bonferroni method to control the overall experiment-wise error rate.

To explore factors associated with anxiety and depression, bivariate analysis between non-normally distributed continuous variables were assessed using Spearman's rho

correlation coefficients. Separate standard multiple regression models were used to identify factors independently associated with anxiety and depression at different time points (4, 8 and 12-month follow-up). The independent and control variables in the regression models were selected based on the extant literature and included 1) sex 2) excess alcohol use 3) baseline KCCQ score 4) baseline ESAS score 5) antidepressant use and 6) history of depression. Additional independent and control variables were selected based on the results of bivariate analysis.

Sample size requirements were estimated using guidance which asserts approximately 15 participants per predictor are required for a well-fitting regression model (Stevens, 1996). Therefore, a sample size of ≥120 participants was required. Multicollinearity was assessed using tolerance values and variance inflation factor (VIF). A tolerance value of <.10 suggests multicollinearity and a VIF value exceeding 10 was regarded as indicating significant multicollinearity (Katz, 2003).

Results

Participant Characteristics

Medical admissions to the Western Infirmary, Glasgow during January 2013 until December 2014 were screened. A total of 313 HF patients were enrolled in the study. Of these 272 (86.9%) completed at least one PROM at baseline and agreed to attend study visits.

Of the 272 participants who completed PROMs at baseline, 63% and 67% had two complete measures, and 34% and 35% had four complete measures on the HADS-A and HADS-D respectively. See Figure 3 for an overview of participants flow through the study.

Figure 3. Participant Flow Through the Study

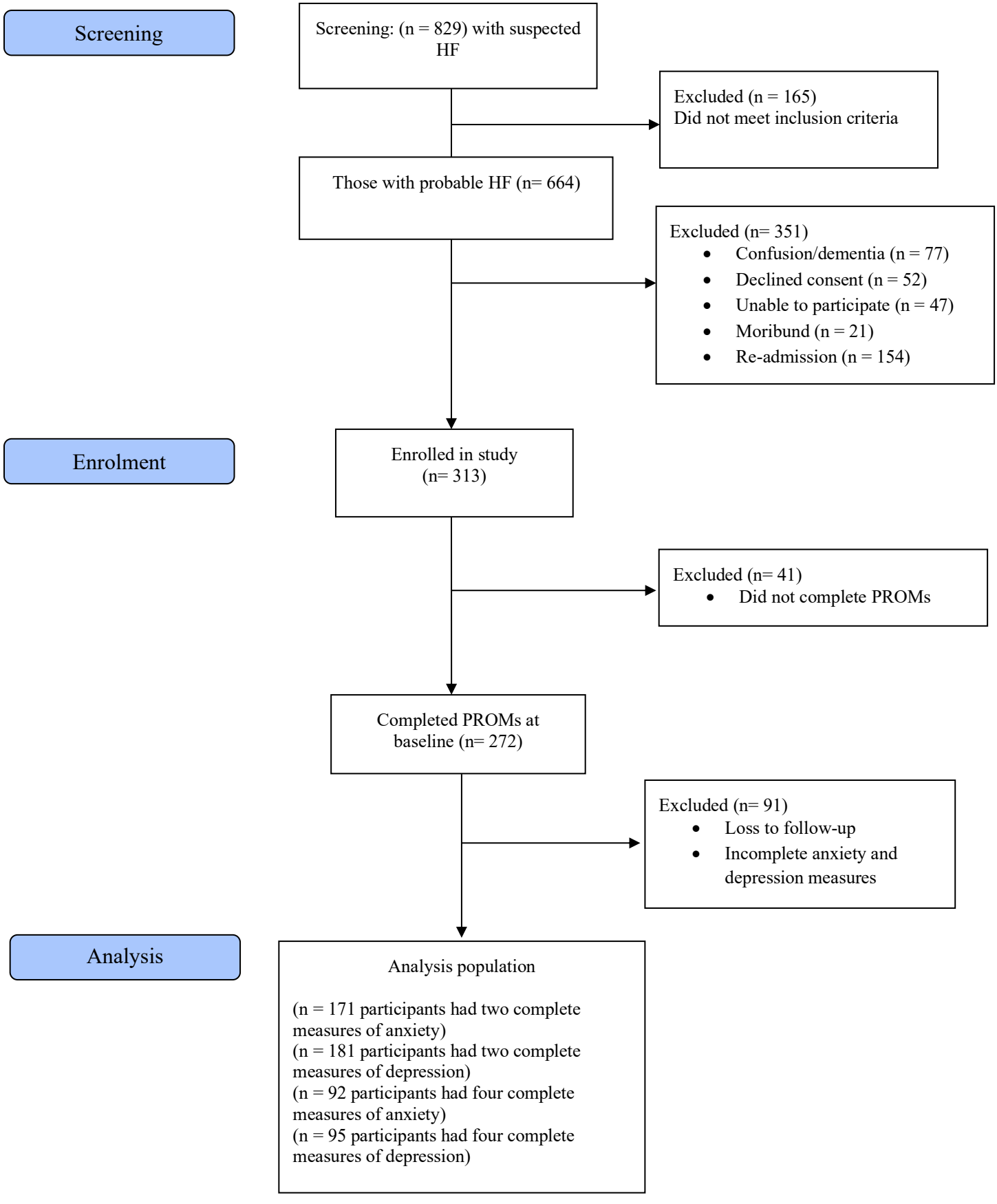


Table 4 shows baseline demographic and clinical characteristics of the sample. The characteristics of participants who completed at least one PROM at baseline were compared with non-completers. Participants who did not complete PROMS at baseline were older (*Md* = 84.24; $p < .001$), were more likely to have a history of cancer χ^2 (1, n = 313) = .4.20, $p = .040$, phi = .130, were less likely to experience wheezing ($p = .022$) or report a history of smoking ($p = .040$) compared to completers.

Table 4 Baseline Demographic and Clinical Characteristics of Participants

	Full Sample N = 313	***Completed PROMS at baseline N = 272***	***Did not complete PROMS at baseline N = 41***	***P-values***
Age	79.88 (70.6, 83.4)	75.99 (69.8, 82.4)	84.24 (79.1, 87.8)	**< .001**
Female Sex	154 (49.2%)	128 (47.1%)	26 (63.4%)	.074
Ethnicity				
South Asian	7 (2.2%)	5 (1.8%)	2 (4.9%)	
Black	1 (0.3%)	1 (0.4%)	0 (0.0%)	.073
White	304 (97.1%)	266 (97.8%)	38 (92.7%)	
Arab/Middle East	1 (.3%)	0 (0%)	1 (2.4%)	
NYHA Class				
Class II	95 (30.4%)	82 (30.1%)	13 (31.7%)	.764
Class III	160 (51.1%)	141 (51.8%)	19 (46.3%)	
Class IV	58 (18.5%)	49 (18%)	9 (22.0%)	
HF Symptoms				
Orthopnoea	232 (74.1%)	204 (75.0%)	28 (68.3%)	.470
Ankle swelling	237 (76.0%)	208 (76.5%)	29 (72.5%)	.726
Palpitations	11 (3.5%)	10 (3.7%)	1 (2.4%)	1.000
Wheezing	65 (20.8%)	62 (22.8%)	3 (7.3%)	**.022**
Paroxysmal nocturnal dyspnoea	221 (70.6%)	194 (71.3%)	27 (65.9%)	.594

HF diagnosis prior to index admission (Yes)	136 (43.5%)	120 (44.1%)	16 (39.0%)	.657
Index Admission Length (Days)	9.00 (5.00, 15.00)	9.00 (5.00, 15.00)	10.00 (5.50, 18.50)	.399
Ejection Fraction				
< 50%	209 (66.8%)	183 (67.3%)	26 (63.4%)	.755
> = 50%	104 (33.2%)	89 (32.7%)	15 (36.6%)	
Atrial Fibrillation History	165 (52.7%)	144 (52.9%)	21 (51.2%)	.970
Myocardial Infarction History	126 (40.3%)	111 (40.8%)	15 (36.6%)	.731
History of Arrythmia	26 (8.3%)	22 (8.1%)	4 (9.8%)	.760
Current Depression	12 (3.9%)†	11 (4.1%)†	1 (2.4%)	1.000
Depression History	43 (13.8%)†	37 (13.7%)†	6 (14.6%)	1.000
Anti-depressant Use	18 (9.4%)†	16 (9.4%)†	2 (10.0%)†	.588
Other Conditions				
Diabetes	100 (31.9%)	89 (32.7%)	11 (26.6%)	.566
Cancer	41 (24.6%)	31 (11.4%)	10 (24.4%)	**.040**
COPD	77 (24.6%)	69 (25.4%)	8 (19.5%)	.537

Smoking History				
Current	55 (17.6%)	51 (18.8%)	4 (10%)	**.040**
Never smoked	174 (55.6%)	143 (52.8%)	31 (77.5%)	
Ex-smoker	82 (26.2%)	77 (28.4%)	5 (12.5%)	
Alcohol History				
None	206 (65.8%)	172 (63.2%)	34 (82.9%)	.103
Excess	13 (4.2%)	13 (4.8%)	0 (0.0%)	
Previous excess	20 (6.4%)	19 (7.0%)	1 (2.4%)	
Within recommended	74 (23.6%)	68 (25.0%)	6 (14.6%)	

Note: Categorical variables are denoted as N and (%) Continuous variables are represented by Median and (Interquartile Range). P values were calculated using Mann Whitney U test for non-normally distributed continuous variables and the chi-square test of association for categorical variables. If the frequency in a cell was <5, p-values were calculated using Fishers exact probability test. For variables with a 2 by 2 table Yates' Correction for Continuity value is presented. ***Bolded*** *values highlight statistically significant differences. † Denotes that valid percentages are reported.*

Tables 5 & 6 in Appendix 2.5, p.166-169 describe the demographic and clinical characteristics of participants with one, two, three and four complete measurements of anxiety and depression. The baseline characteristics of participants who completed the HADS at baseline were compared to those with two, three and four complete measurements.

Participants who provided four measures of anxiety were more likely to have been diagnosed with CHF prior to the index admission χ^2 (3, n = 233) = 7.847, p = .049, phi = .184 compared to participants who completed HADS-A at baseline only. There was a significant association between baseline anti-depressant use and HADS-D completion status (p = .026). A higher proportion of participants with two complete measures of depression (at baseline and 4-months) were prescribed anti-depressant medication compared to participants with four complete measures (20.9% vs 6.3% respectively). Participants who completed HADS-D at baseline were more likely to report no alcohol use compared to participants with four complete measures (p = .012*).*

There was a trend, although not statistically significant for a lower proportion of participants with higher NYHA class (Class IV) to provide four HADS-D measurements, χ^2 (6, n = 238) = 12.517, p = .051, phi = .229. Specifically, 21.1% of participants who completed HADS-D at baseline only were classified as NYHA Class IV compared to 8.4% of participants who had four complete depression measures.

Anxiety and Depression Over Time

Participants' anxiety scores at baseline, 4, 8 and 12-months were non-normally distributed, with skewness values of: .631 (*SE* = .251), .839 (*SE* = .251), 1.119 (*SE* = .251), and .919 (*SE* = .251) respectively. Depression scores at baseline, 4, 8 and 12-months were also non-normally distributed, with skewness values of: .531 (*SE* = .247), .517 (*SE* = .247), .796 (*SE* = .247) and .782 (*SE* = .247) respectively. Inspection of histograms (See Appendix 2.6, p.170-171) indicated anxiety and depression scores were positively skewed.

Anxiety

There was a statistically significant difference in HADS-A scores across the four time points (baseline, 4, 8 and 12-month follow-up) χ^2 (3, n = 92) = 18.514, p <.001. Post-hoc pairwise comparisons were conducted using four Wilcoxon Signed Rank tests, applying the Bonferroni adjustment to correct for problems caused by multiple comparisons (corrected alpha = .0125). Results indicated a statistically significant reduction in anxiety scores from baseline to 4-months, z = -2.520, p = .012, with a small effect size (r = 0.19). Anxiety scores did not differ significantly between 4- and 8-month follow-up, z = -.233, p = .816 or between 8 and 12-month follow-up, z = -2.042, p = .041. There was a significant reduction in anxiety scores from baseline to 12-month follow-up, -4.088, p < .001, with a medium effect size (r = 0.30). As can be seen in Table 7 the median score on the HADS-A scale decreased from baseline (*Md* = 6) to 4-month follow-up (*Md* = 4) and 12-month follow-up (*Md* = 3).

Depression

There were no statistically significant differences in HADS-D scores across the four time points (baseline, 4, 8 and 12-month follow-up) χ^2 (3, n =95) = 2.957, p = .398. As can be seen from Table 7 the median score on the HADS-D remained stable (*Md* = 6) between baseline, 4 and 8-month follow-up.

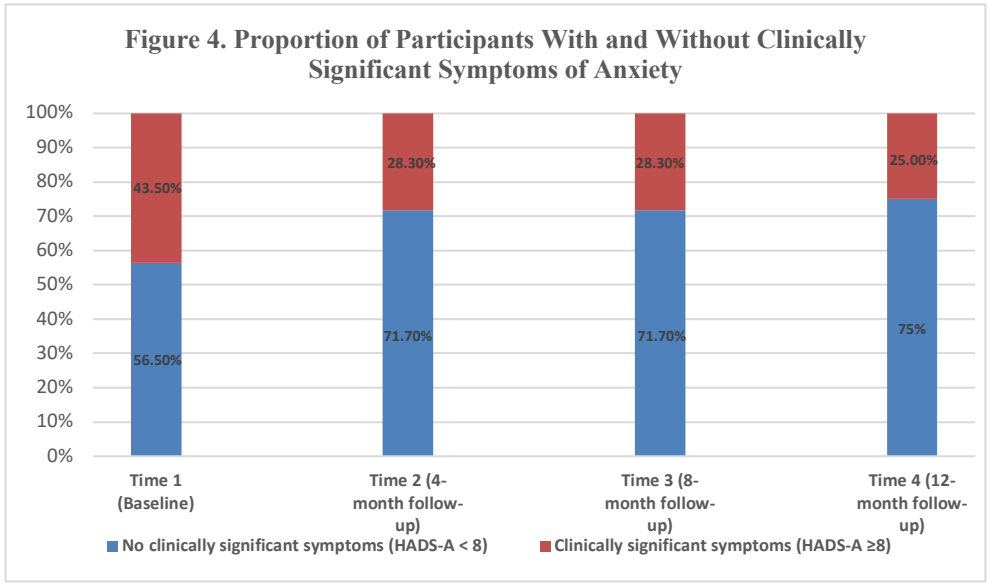
Table 7 Medians (MD) and Interquartile Range (IQR) for Participants Symptoms of Anxiety and Depression at Baseline (Time 1), 4-Month (Time 2), 8-Month (Time 3) and 12-Month Follow-up (Time 4).

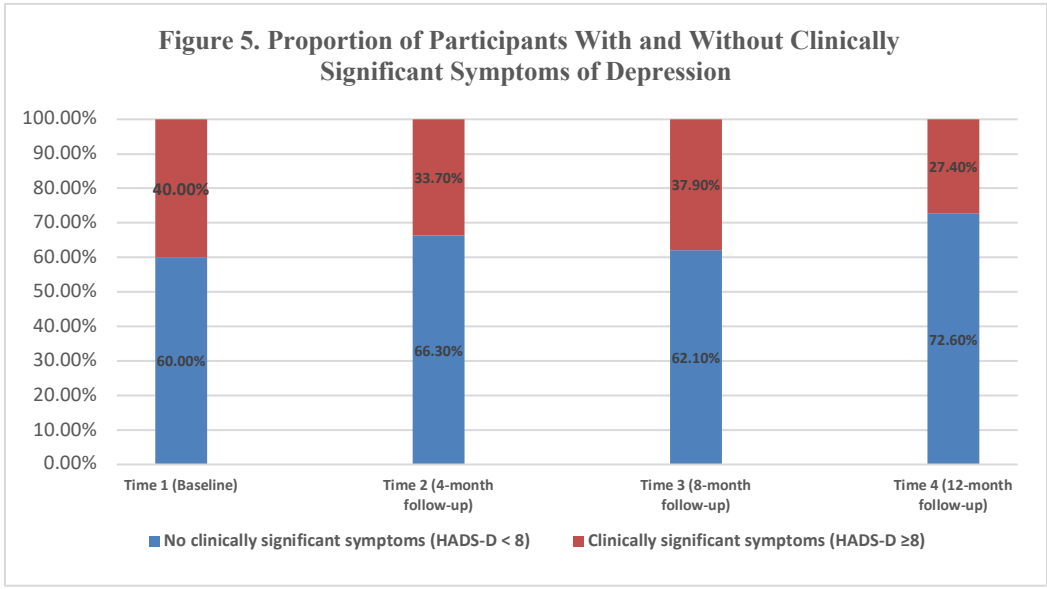
	TIME 1 MD (IQR)	**TIME 2 MD (IQR)**	**TIME 3 MD (IQR)**	**TIME 4 MD (IQR)**
HADS-A TOTAL SCORE	6.00 (3.25, 9.00)	4.00 (2.00, 9.00)	5.00 (2.00, 8.00)	3.00 (3.00, 7.75)
HADS-D TOTAL SCORE	6.00 (3.00, 9.00)	6.00 (2.00, 10.00)	6.00 (3.00, 9.00)	5.00 (2.00, 8.00)

To examine if there were significant changes in the proportion of participants with and without clinically significant anxiety and depression over time (baseline, 4, 8 and 12-month follow-up) related samples Cochran's Q tests were conducted. There was a statistically significant difference in the proportion of participants with clinically significant anxiety symptoms over time, χ^2 (3) = 19.97, p <.001. Pairwise comparisons, indicated significant differences between time 1 (baseline) and time 2 (4-month follow-up) (p = .005), time 1 (baseline) and time 3 (8-month follow-up) (p = .005) and time 1 (baseline) and time 4 (12-month follow-up) (p < .001). As can be seen in Figure 4 the proportion of participants reporting clinically significant symptoms of anxiety decreased from 43.5% at baseline to 25.0% at 12-month follow-up.

Results also revealed a significant difference in the proportion of participants with clinically significant depression symptoms over time, χ^2 (3) = 8.13, p = .04. Pairwise comparisons, indicated significant differences between time 1 (baseline) and time 4 (12-month follow-up) ($p < .01$) and time 3 (8 month) and time 4 (12-month follow-up) (p = .028). As can be seen in Figure 5 the proportion of participants reporting clinically significant depression symptoms decreased from 40.0% at baseline to 27.40% at 12-months.

Figure 4 & 5 Proportion of Participants With and Without Clinically Significant Anxiety and Depression Symptoms at Baseline (Time 1), 4-Month (Time 2), 8-Month (Time 3) and 12-Month Follow-up (Time 4)





Trajectories of Anxiety and Depression

Using an approach described in previous research (Dekker et al., 2011), participants were assigned to one of four symptom status groups based on the change of their HADS score at baseline compared to 4-, 8- and 12-month follow-up (See Table 3).

As can be seen from Figure 6, 7 and 8 from baseline to 4, 8 and 12-month follow-up between 48-50 participants remained anxiety symptom free, while 17-20 experienced improvement in their anxiety symptoms, 2-4 had developed anxiety symptoms, and 20-23 reported persistent anxiety symptoms.

Additionally, review of Figures 9, 10 and 11 depicts that from baseline to 4, 8 and 12-month follow-up between 48-51 participants remained depression symptom free, while 11-18 experienced improvement in their depression symptoms, 6-9 had developed depression symptoms, and 20-27 reported persistent depression symptoms.

Figure 6. Anxiety Symptom Status Change from Baseline to 4-month Follow-up

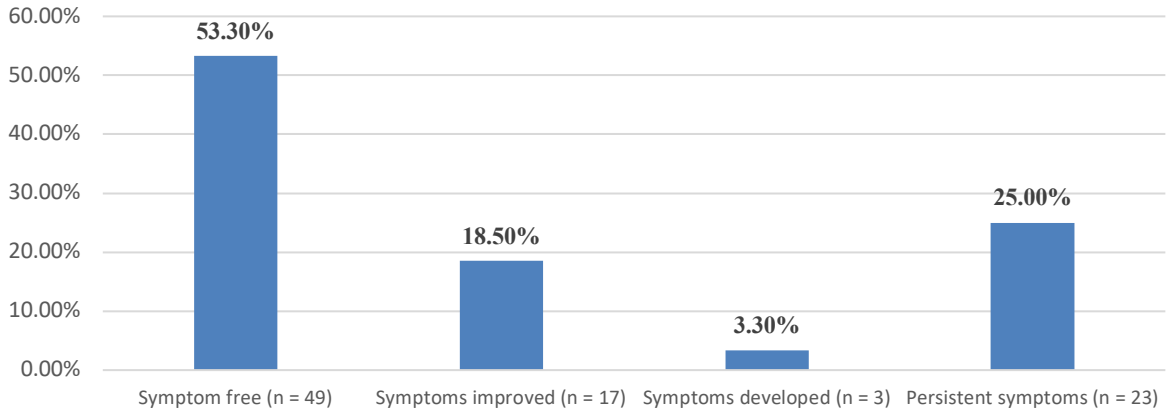


Figure 7. Anxiety Symptom Status Change from Baseline to 8-Month Follow-up

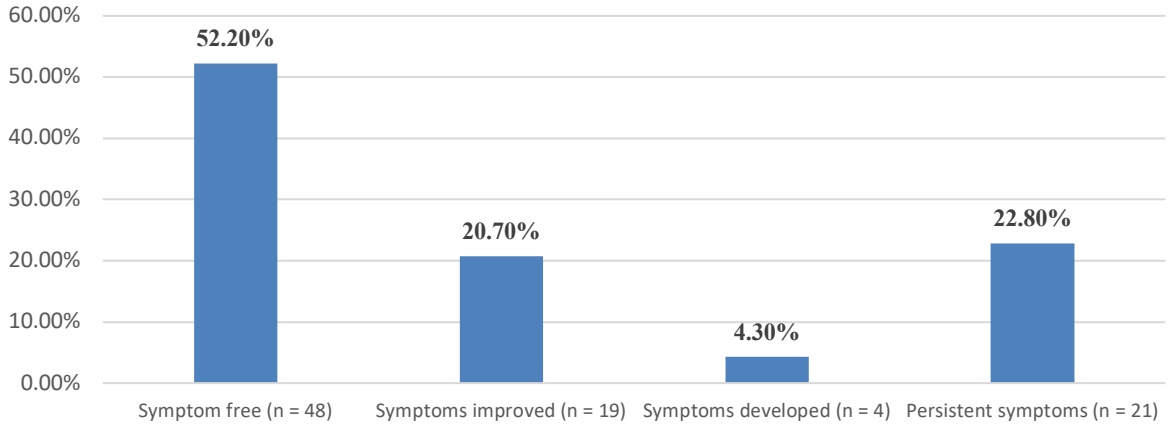


Figure 8. Anxiety Symptom Status Change from Baseline to 12-Month Follow-up

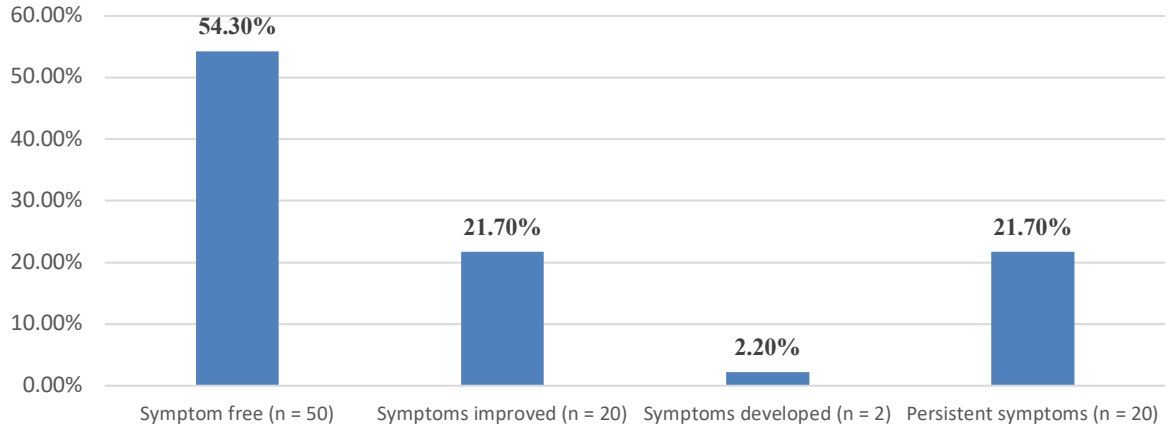


Figure 9. Depression Symptom Status Change from Baseline to 4-month Follow-up

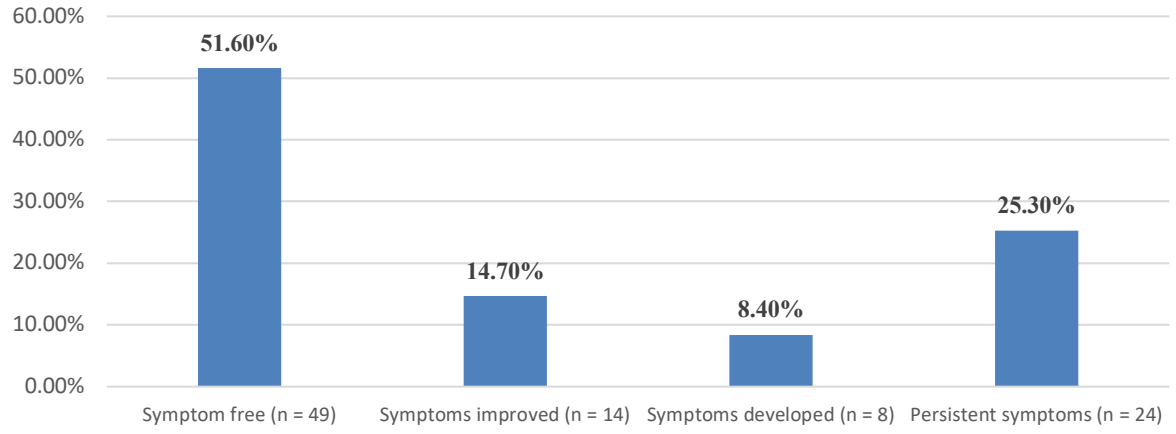


Figure 10. Depression Symptom Status Change from Baseline to 8-Month Follow-up

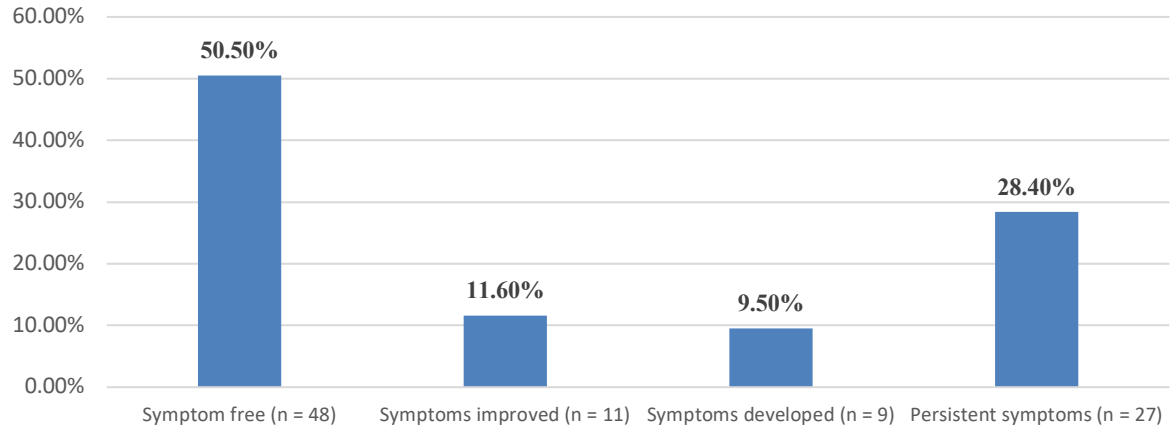
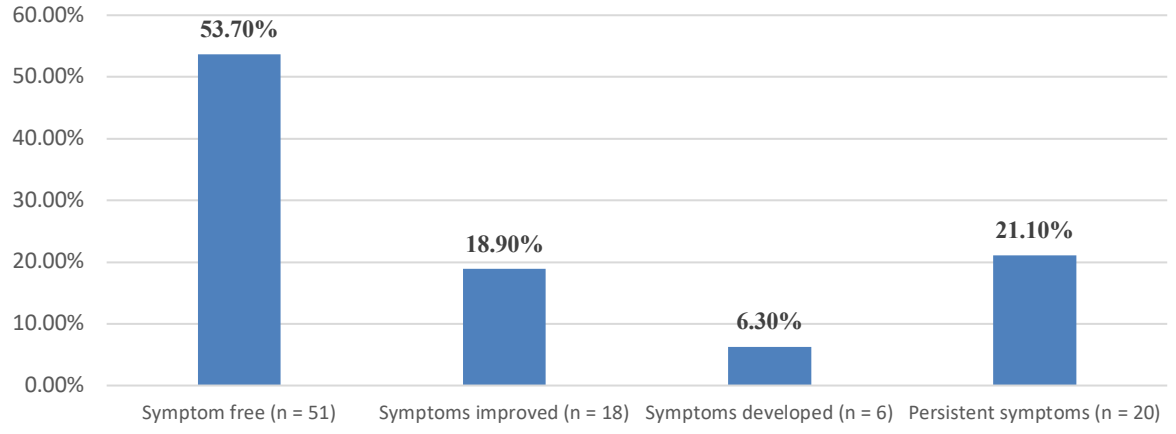


Figure 11. Depression Symptom Status Change from Baseline to 12-Month Follow-up



Factors Associated with Anxiety and Depression

Results of bivariate correlations between continuous variables using Spearman's rho correlation coefficients are presented in Table 8.

Table 8 Correlation Coefficients Among Continuous Variables

	Age	Baseline anxiety score	Baseline depression score	Anxiety score (4-months)	Depression score (4-months)	Anxiety score (8-months)	Depression score (8-months)	Anxiety score (12-months)	Depression score (12-months)	Baseline symptom burden
Age										
Baseline anxiety score	.117									
Baseline depression score	.206**	.525**								
Anxiety score at 4-months	.122	.634**	406**							
Depression score at 4-months	.122	.391**	.612**							
Anxiety score at 8-months	.044	643**	.353**							
Depression score at 8-months	.002	.445**	.647**							
Anxiety score at 12-months	.052	.570**	.280**							
Depression score at 12-months	-.055	222*	.600**							
Baseline symptom burden score (ESAS)	.127	.467**	.452**	.413**	.332**	.387**	.338**	.435**	.294**	
Baseline KCCQ summary score	-.107	-.379**	-.531**	-.220**	-.357**	-.226*	-.417**	-.249*	-.397**	-.496**

*p<.05
**p<.01

Predictors of Anxiety and Depression

The dependent variables anxiety and depression scores at 4-month, 8-month and 12-month follow-up were regressed on eight independent and control variables (anti-depressant use, history of depression, sex, excess alcohol use, baseline anxiety and depression score, baseline symptom burden and baseline KCCQ summary score), using standard multiple regression. The variables were entered into the model simultaneously. Preliminary analyses were conducted to ensure no violation of the assumptions of normality of residuals, linearity, multicollinearity, and homoscedasticity.

Predictors of Anxiety and Depression at 4-month follow-up

The results of the anxiety model were significant: F (8, 162), = 20.323, $p < .001$. Adjusted R^2 was found to be .476, indicating the model accounted for 47.5% of the variance in participants anxiety scores at 4-months. As can be seen from table nine, baseline KCCQ summary score (standardised $\beta = .225$, $p < .01$) and baseline anxiety score (standardised $\beta = .616$, $p < .001$) independently predicted anxiety at 4-months.

The results of the depression model were also significant: F (8, 168), = 15.21, $p = < .001$. Adjusted R^2 was found to be .392, indicating the model accounted for 39.2% of the variance in participants depression scores at 4-months. As can be seen from table nine, depression score at baseline (standardised $\beta = -601$, $p < .001$) and anti-depressant use (standardised $\beta = .150$, $p = .015$) independently predicted depression at 4-month follow-up.

Predictors of Anxiety and Depression at 8-month follow-up

The results of the anxiety model were significant: F (8, 139), = 17.662, $p < .001$. Adjusted R^2 was found to be .476, indicating the model accounted for 47.5% of the variance in participants anxiety scores at 8-months. As can be seen from table nine, baseline anxiety (standardised β =.620, $p < .001$) and depression history (standardised β = .277, $p = <$ .001) independently predicted participants anxiety at 8-month follow-up.

Additionally, the results depression model was significant: F (8, 141), = 13.636, $p < .001$. Adjusted R^2 was found to be .397, indicating overall the model accounted for 39.7% of the variance in participants depression scores at 8-months. As can be seen from table nine, depression score at baseline (standardised β = .489, $p < .001$) and history of depression (standardised β = .134 $p = .038$) independently predicted depression at 8-months.

Predictors of Anxiety and Depression at 12-month follow-up

The results of the anxiety model were significant: F (8, 115), = 12.730, $p < .001$. Adjusted R^2 was found to be .433, indicating overall the model accounted for 43.3% of the of the variance of in participants anxiety scores at 12-months. As can be seen from table nine, female sex (standardised β = -.162, $p = .025$), depression history (standardised β = .163, $p = .020$) and baseline anxiety score (standardised β = .591, $p < .001$) independently predicted anxiety at 12-months.

Additionally, the results of the depression model were significant: F (8, 122), = 9.423, $p < .001$. Adjusted R^2 was found to be .356, indicating overall the model accounted for 35.6% of the variance in participants depression scores at 12-months. As can be seen from table nine, female sex (standardised $\beta = -.226$, $p = .004$), and baseline depression score (standardised $\beta = .552$, $p < .001$) independently predicted depression at 12-months.

Table 9 Variables Associated with Anxiety and Depression

	Variable	Standardised β	t	95% CI	*p*-value
Dependent Variable: Anxiety at 4-months	Female vs Male sex	.008	.142	-.952–1.099	.887
	Excess alcohol use	.107	1.890	-.110–4.989	.061
	Baseline ESAS score	.135	1.857	-.002–.059	.065
	Baseline KCCQ summary score	.225	3.100	.018–.080	**.002**
	Anti-depressant use	.081	1.402	-.643–3.793	.163
	Depression history	.080	1.421	-.412–2.527	.157
	Baseline anxiety	.616	8.483	.460–.739	**< .001**
	Baseline depression	.108	1.387	-.051–.292	.167
Dependent Variable: Depression at 4-months	Female vs Male sex	-.044	-.721	-1.393–.648	.472
	Excess alcohol use	.047	.791	-1.522–3.556	.430
	Baseline ESAS score	.012	.152	-.028–.032	.880
	Baseline KCCQ summary score	.044	.573	-.022–.040	.567
	Anti-depressant use	.150	2.469	.554–4.972	**.015**
	Depression history	.082	1.379	-.441–2.486	.170
	Baseline anxiety	.039	.502	-.104–.174	.617
	Baseline depression	.601	7.31	.461–.803	**<.001**

	Variable	Standardised β	t	95% CI	P-value
Dependent Variable: Anxiety at 8-months	Female vs Male sex	-.005	-.075	-1.171–1.085	.941
	Excess alcohol use	.081	1.322	-.930– 4.680	.188
	Baseline ESAS score	.137	1.754	-.004–.063	.082
	Baseline KCCQ summary score	.135	1.731	-.004–.064	.086
	Anti-depressant use	.011	.174	-2.226– 2.656	.862
	Depression history	.277	3.742	1.444 – 4.678	**< .001**
	Baseline anxiety	.620	7.945	.464 –.771	**< .001**
	Baseline depression	.046	.547	-.136–.241	.586
Dependent Variable: Depression at 8-months	Female vs Male sex	-.055	-.843	-1.629–.655	.401
	Excess alcohol use	.040	.619	-1.950–3.730	.537
	Baseline ESAS score	.044	.534	-.025–.043	.594
	Baseline KCCQ summary score	.-.050	-.600	-.045–.024	.550
	Anti-depressant use	.057	.869	-1.385– 3.557	.386
	Depression history	.134	2.092	.095– 3.369	**.038**
	Baseline anxiety	.138	1.667	-.024–.287	.098
	Baseline depression	.489	5.528	.343–.725	**< .001**

	Variable	Standardised β	t	95% CI	P-value
Dependent Variable: Anxiety at 12-months	Female vs Male sex	-.162	-2.269	-2.802 – -.190	**.025**
	Excess alcohol use	-.026	-.370	-2.512–1.721	.712
	Baseline ESAS score	.162	1.817	-.003–.073	.072
	Baseline KCCQ summary score	.153	1.725	-.005–.073	.087
	Anti-depressant use	.000	-.007	-2.775–2.756	.995
	Depression history	.163	2.364	.354–4.012	**.020**
	Baseline anxiety	.591	6.668	.411–.759	**< .001**
	Baseline depression	.076	.800	-.128–.301	.425
Dependent Variable: Depression at 12-months	Female vs Male gender	-.226	-2.965	-3.195– -.635	**.004**
	Excess alcohol use	-.022	-.288	-2.375–1.772	.774
	Baseline ESAS score	.038	.399	-.030–.045	.690
	Baseline KCCQ summary score	-.041	.-.435	-.046–.030	.664
	Anti-depressant use	.095	1.259	-.987–4.431	.211
	Depression history	.038	.510	-1.330–2.253	.611
	Baseline anxiety	-.025	-.259	-.193–.148	.796
	Baseline depression	.552	5.430	.365–.785	**< .001**

Discussion

The primary aim of the study was to examine and describe the trajectories of anxiety and depression in patients with CHF over 12-month follow-up. At the group level, there were significant reductions in median anxiety scores between baseline (index admission) and 4 and 12-month follow-up. There was also a significant decrease in the proportion of participants reporting clinically significant anxiety from baseline/index admission (43.5%), compared to (25.0%) at 12-months. Additionally, more than half of the sample remained anxiety 'symptom' free during follow-up and one in five participants, who reported anxiety at baseline experienced symptom resolution (scores fell below HADS cut-off) by 4 to 12 months. This pattern may be indicative of a transient adjustment response, with higher rates of anxiety at baseline representing an emotional reaction to hospitalisation or decline in health/functioning. These findings are consistent with the working model of adjustment (Moss-Morris, 2013) which asserts critical events including hospitalisation, diagnosis or relapse/disease progression disrupts an individual's 'emotional equilibrium' leading to distress.

Results also indicated 25% of the sample reported anxiety symptoms at 12-months, and between 21.7% to 25% of participants, who reported clinically significant anxiety at baseline experienced persistent symptoms across follow-up phases. Furthermore, a small proportion between 2.2% to 4.3% developed anxiety during the follow-up period. These findings are consistent with previous research which found approximately 30% of people with CHF report clinically significant anxiety symptoms (based on self-report measures) (Easton et al., 2016).

In terms of depression, there were no statistically significant reductions in participants median depression scores at baseline (index admission) and 4, 8 and 12-month follow-up. Nevertheless, results showed a significant decrease in the proportion of participants reporting clinically significant depression symptoms from their index admission (baseline) 40.0% compared to 27.4% at 12-months. This finding is consistent with research reporting higher rates of depression among people hospitalised with CHF compared to outpatients experiencing a period of stability in their HF symptoms (Konstam et al., 2005).

Additionally, over half of the sample, remained depression 'symptom free', and 14.7%, 11.6% and 18.9% who reported depression symptoms at baseline experienced symptom resolution by 4-, 8- and 12-month follow-up respectively. This pattern could be indicative of a transient adjustment response, with higher rates of depression at baseline representing an emotional reaction to a critical event (e.g., hospitalisation, receiving a diagnosis or disease progression) (Moss-Morris, 2013).

These findings are consistent with results from a previous study which examined the trajectories of depression in a sample of inpatients and outpatients with CHF. Dekker and colleagues (2011) found 64% of the sample were classified as 'depressive symptom free', and 15% of participants who reported depression at baseline recovered after three to six months.

Results also revealed 6.3% of participants who were 'depressive symptom free' at baseline reported a clinically significant increase in symptoms at 12-month follow-up. These findings are consistent with Dekker and colleagues (2011) study which found 6%

had developed symptoms of depression at 3-or 6-month follow-up. For participants who reported clinically significant symptoms of depression at baseline, between 21.1% and 28.4% experienced persistent symptoms of depression at 12-month and 8-month follow-up respectively. The proportion of the sample experiencing persistent depression is higher than one study reporting 15% of CHF patients experienced persistent depression (Dekker et al., 2011), and lower than Johansson and colleagues (2013) study which found 39% reported persistent depression. The difference in findings between the present study and the aforementioned research may be explained by variance in the duration of follow-up, sample size and self-report measures used to assess depression across the studies.

The second aim of this study was to identify demographic and clinical factors that were independently associated with anxiety and depression in CHF patients during 12-month follow-up. Results showed baseline KCCQ summary score, baseline anxiety score (at 4-month follow-up), baseline anxiety and history of depression (at 8-month follow-up) and female sex, history of depression and baseline anxiety (at 12-month follow-up) independently predicted anxiety. These findings are consistent with studies which found reduced HR-QoL, and presence or history of depression predicted anxiety CHF patients (Allabadi et al., 2019; Årestedt et al., 2014).

In terms of depression, factors including baseline depression score and anti-depressant use (at 4-month follow-up), history of depression (at 8 month-follow-up) and female sex and baseline depression (at 12-month-follow-up) predicted depression. These findings are consistent with previous research which found premorbid factors including past

history of distress and anti-depressant treatment predicted depression outcome trajectory in CHF patients at 12-week follow-up (Koenig et al., 2006).

Nevertheless, the results are not consistent with research which found behavioural factors including (excess alcohol use) and baseline HR-QoL predicted depression at 12-month follow-up in HF patients (Havranek et al., 2004). The mixed findings may be partially explained by differences between the samples. In the present study a relatively low proportion (6.3% of participants with four complete depression measurements) reported excess alcohol use compared to between 11.4% to 23.1% of the sample recruited by Havranek and colleagues (2004).

Strengths

This study has a number of strengths. First, the data used in this secondary analysis were collected by approaching a largely consecutive cohort of patients hospitalised for suspected CHF (Campbell et al, 2015), which reduced the risk of selection bias.

Second, the recruited sample included a relatively equal number of men and women participants. This is a key strength as although data have shown the incidence of CHF is similar among men and women (Go et al., 2014), women are underrepresented in studies of HF (Pressler, 2016). Consequently, there is increased confidence the study's findings can be extrapolated to female CHF populations. Additionally, the present study addressed some of the limitations of previous research by simultaneously describing the time-course of anxiety and depression in CHF patients, as opposed to previous research focusing on depression only (Volz et al., 2011).

Limitations

A number of limitations of the study must be acknowledged and the findings should be interpreted with caution. First, a considerable number of participants were excluded from the analysis due to not having complete data on baseline or follow-up measurements of anxiety and depression. It has been acknowledged longitudinal studies are prone to incomplete data/participant drop out as procedures including completing outcome measures or attending study visits can become more demanding for participants as their CHF progresses (Campbell et al., 2015).

Analysis revealed a lower proportion of participants with four measures of depression used anti-depressant medication compared to participants who had two complete measures. There was also a trend, although not statistically significant, for a lower proportion of participants with four complete measures of depression and anxiety to be classified as NYHA Class IV compared to participants who had completed measures at baseline. This may have resulted in a bias towards participants who experienced less severe CHF symptoms/functional limitations or levels of emotional distress. Therefore, the findings may not be generalisable to CHF patients experiencing the most severe functional limitations or those with levels of emotional distress requiring psychotropic medication.

Nevertheless, analysis revealed no significant differences in the proportion of participants who reported anxiety and depression at baseline (defined as HADS ≥8) between participants completing one measure of anxiety and depression and those providing four measures. There were no significant differences on demographic and clinical characteristics including age, sex, presence of HF symptoms, history of

depression, baseline symptom burden, cardiac factors (e.g., history of arrythmias) and presence of co-occurring health issues (e.g., diabetes). Therefore, reducing concerns of presence of wider systematic bias.

Second, most participants were Caucasian, and the findings might not be generalisable to other ethnic groups. Additionally, participants who did not complete outcome measures at baseline were older compared to completers. This is consistent with general issues in the HF literature which notes although HF is more common in people aged 80 or older (Go et al., 2014), the mean age of people recruited in CHF studies was 61.4 years (Heiat, Gross & Krumholz, 2002). The median age of participants completing four measures of anxiety was 74, suggesting older adults were represented in this sample. Nevertheless, the results may not generalise to older adults (over the age of 75).

Third, the data analytic methods used to describe the time-course of anxiety and depression symptoms over time have limitations. Some assert the examination of overall change in anxiety or depression scores at the group level, assumes all participants recover in a homogenous, linear fashion (Murphy et al., 2008). It is conceivable while anxiety and depression improves over time for the majority of patients, for others emotional distress may persist or worsen over-time. Therefore, the statistical methods in this study were limited because they did not enable recognition of multiple trajectories of change in distress over-time.

Similarly, the current study's examination of change in the proportion of participants presenting with clinically significant anxiety and depression over time and assignment of participants into four symptom status change groups has limitations. This method does

not allow the identification or characterisation of multiple trajectories of change in anxiety and depression over time (Murphy et al., 2008). The study also relied on applying a clinical cut off (≥8 on the HADS) to 1) classify participants as having clinically significant anxiety and depression and 2) allocate participants into one of the four symptom status change groups. Some assert the use of cut offs might not accurately reflect or provide a nuanced picture of change in the patients' experience (Murphy et al., 2008).

Finally, as this was a secondary data analysis, there was no available information on participants' history of anxiety or past treatment with psychological therapy. There was also no data collected on psychosocial factors which may influence emotional adjustment in CHF populations including coping styles and cognitive illness perceptions. Consequently, the exploration of factors associated with anxiety or depression was restricted to non-modifiable clinical and demographic characteristics.

Research Implications

The present study identified some clinical risk factors (history of depression or psychotropic medication use), which predicted distress in this cohort of CHF patients. Future research is required to identify the demographic, social or psychological factors (e.g., cognitive appraisals), which might mediate the relationship between clinical history factors and emotional adjustment to CHF.

Future research in this area should be underpinned by theoretical models of emotional adjustment to chronic illness. As this study was a secondary analysis, the outcome measures analysed were selected due to availability of data as opposed to being guided by psychological models of adjustment. Further research is required to test out predictions of the working model of adjustment including the influence that social/environmental factors, cognitive factors and behavioural factors (Moss-Morris, 2013) have on the emotional adjustment trajectories of CHF patients. Future research could measure operationalised variables including presence of social support, socio-economic status, perceptions of stress, negative illness representations (e.g., perceptions of control), avoidant coping and experiential avoidance/repression of emotions using validated measures. Collecting data on these factors may help to explain individual differences in emotional adjustment trajectories following hospital admission in CHF patients.

Some social, cognitive and behavioural factors are potentially modifiable and future research examining the relationship between these factors, critical events/on-going illness stressors and emotional outcomes could elucidate the psychosocial characteristics of patients at greater risk for prolonged distress and inform targets for supportive interventions.

Additionally, as described above the data analytic methods used in this study have limitations. Future research could consider using techniques such as latent class analysis or growth modelling techniques to identify and describe multiple or non-linear trajectories of change in anxiety and depression in CHF patients over time. Characterising and understanding anxiety and depression symptom trajectories and the

factors/characteristics associated with these trajectories is required to inform the optimal timing of screening for emotional distress, and to inform preventative strategies to improve CHF patients' quality of life.

Finally, a larger multi-centre study, recruiting participants from Black, Asian and Minority Ethnic backgrounds is required to replicate the findings and to enhance the cultural validity and generalisability of the findings.

Conclusion

To conclude, this study found a significant reduction in the proportion of CHF patients reporting anxiety and depression symptoms from baseline (hospital admission for HF) to 12-month follow-up. This may be indicative of a transient adjustment response, with higher rates of anxiety and depression observed at baseline representing an emotional reaction to hospitalisation or decline in health/functioning. There was also a subset of participants that experienced persistent anxiety and depression symptoms during follow-up, while a small proportion who were 'symptom free' at baseline went on to develop anxiety and depression.

Relevance to Clinical Practice

The findings of this study contribute to the literature by describing the trajectory of anxiety and depression symptoms in people with CHF, a subject which has been relatively neglected (Voltz et al., 2011; Johansson et al., 2013). Overall, results indicated most participants remained anxiety and depression symptom free or experienced resolution in their anxiety and depression symptoms during follow-up. Nevertheless, there was a proportion of participants who experienced persistent anxiety and depression symptoms during 12-month follow-up. Accordingly, routine and repeated screening, for anxiety and depression in outpatient settings or primary care may be warranted to identify CHF patients who do not experience a transient adjustment response following hospitalisation. Additionally, findings revealed: history of depression, female sex and HR-QoL at baseline predicted anxiety during follow-up. While, female sex, history of depression and anti-depressant use predicted depression during the follow-up period. Therefore, it may be most critical to screen for anxiety and depression among female CHF patients, or people with a history of depression, anti-depressant use and reduced HR-QoL.

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Appendix 1.1 – Author Publication Guidelines for Journal of Clinical Nursing

Aims and Scope

The Journal of Clinical Nursing (JCN) is an international, peer reviewed, scientific journal that seeks to promote the development and exchange of knowledge that is directly relevant to all spheres of nursing practice. The primary aim is to promote a high standard of clinically related scholarship which advances and supports the practice and discipline of nursing. The Journal also aims to promote the international exchange of ideas and experience that draws from the different cultures in which practice takes place. Further, JCN seeks to enrich insight into clinical need and the implications for nursing intervention and models of service delivery. Emphasis is placed on promoting critical debate on the art and science of nursing practice.

JCN is essential reading for anyone involved in nursing practice, whether clinicians, researchers, educators, managers, policy makers, or students. The development of clinical practice and the changing patterns of inter-professional working are also central to JCN's scope of interest. Contributions are welcomed from other health professionals on issues that have a direct impact on nursing practice.

Review Articles

- *Abstract:* 300 words maximum. Structured under the sub-headings: Aims and objectives; Background, Design; Methods; Results (do not report p values, confidence intervals); Conclusions, and Relevance to clinical practice.
- *Word limit*: 8,000 words maximum (quotations are included in the overall word count of articles, and abstract, references, tables and figures are excluded).
- *Main text structure:* Review Articles should be structured, under the sub-headings: Introduction, Aims, Methods, Results, Discussion, Conclusion, and Relevance to Clinical Practice.
- *References:* 50 maximum; all references must be available in English.

General Style Points

The following points provide general advice on formatting and style.

- **Abbreviations:** In general, terms should not be abbreviated unless they are used repeatedly.
- **Units of measurement:** Measurements should be given in SI or SI-derived units.
- ***Tables***
  Tables should be self-contained and complement, information contained in the text. They should be supplied as editable files, not pasted as images. Legends should be concise but comprehensive – the table, legend, and footnotes must be understandable without reference to the text. All abbreviations must be defined in footnotes. Footnote symbols: †, ‡, §, ¶, should be used (in that order) and *, **, *** should be reserved for P-values.
- **References-** References should be prepared according to the Wiley APA Manual Style.

Full Details are available at:
https://onlinelibrary.wiley.com/page/journal/13652702/homepage/forauthors.html#editorial
(Last accessed on 13th of February 2021)

Appendix 1.2 Search Strategy and Terms

CINAHL
Searched 24th of July 2020

1	MH (MH "Anxiety") OR (MH "Anxiety Disorders") (MH "Depression") OR (MH "Depression, Reactive") OR (MH "Dysthymic Disorder") OR (MH "Affective Symptoms") OR (MH "Affective Disorders" OR (MH "Adaptation, Psychological") OR (MH "Adjustment Disorders") OR (MH "Stress, Psychological") OR (MH "Psychological Well-Being") OR (MH "Psychosocial Aspects of Illness") OR (MH "Stress") OR (MH "Stress, Psychological") OR (MH "Psychosocial Aspects of Illness") OR (MH "Mental Disorders") OR (MH "Mental Disorders, Chronic") OR (MH "Behavioral and Mental Disorders") OR (MH "Mental Health")
2	TI (anxi* or depress* or mood disorder* or emotion* or psych* or (mental n2 status) or (affective n2 disorder*) or (low n2 mood) or dysthymia or distress or stress or (mental n2 health) or (mental n2 illness) or (mental n2 wellbeing) or (mental n2 disorder*) or (psychological n2 adjustment) or (emotional n2 adjustment) or (adjustment n2 disorder) or (emotional n2 adaptation)) OR AB (anxi* or depress* or mood disorder* or emotion* or psych* or (mental n2 status) or (affective n2 disorder*) or (low n2 mood) or dysthymia or distress or stress or (mental n2 health) or (mental n2 illness) or (mental n2 wellbeing) or (mental n2 disorder*) or (psychological n2 adjustment) or (emotional n2 adjustment) or (adjustment n2 disorder) or (emotional n2 adaptation))
3	S1 OR S2
4	MH (MH "Defibrillators, Implantable") OR (MH "Defibrillators, Automated External")
5	TI (((Implantable cardioverter defibrillator or ((implantable or internal or automatic or automated) n2 (cardioverter or defibrillator)) or AICD or ICD).)) OR AB (((Implantable cardioverter defibrillator or ((implantable or internal or automatic or automated) n2 (cardioverter or defibrillator)) or AICD or ICD).))
6	S4 OR S5
7	S3 AND S6
8	Limit 7 to Published Date: 2014-2020 Expanders - Apply equivalent subjects Narrow by Language0: - english Search modes - Boolean/Phrase

MEDLINE Searched 24th of July 2020

1	MH (MH "Anxiety Disorders") OR (MH "Anxiety") OR (MH "Affective Symptoms") OR (MH "Depression") OR (MH "Depressive Disorder") OR (MH "Depressive Disorder, Major") OR (MH "Adjustment Disorders") OR (MH "Dysthymic Disorder") OR (MH "Mood Disorders") OR (MH "Emotional Adjustment" OR (MH "Adaptation, Psychological") OR (MH "Adjustment Disorders") OR (MH "Stress, Psychological") OR (MH "Psychological Distress") OR (MH "Psychopathology") OR (MH "Mental Disorders") OR (MH "Mental Health")
2	TI (anxi* or depress* or mood disorder* or emotion* or psych* or (mental n2 status) or (affective n2 disorder*) or (low n2 mood) or dysthymia or distress or stress or (mental n2 health) or (mental n2 illness) or (mental n2 wellbeing) or (mental n2 disorder*) or (psychological n2 adjustment) or (emotional n2 adjustment) or (adjustment n2 disorder) or (emotional n2 adaptation)) OR AB (anxi* or depress* or mood disorder* or emotion* or psych* or (mental n2 status) or (affective n2 disorder*) or (low n2 mood) or dysthymia or distress or stress or (mental n2 health) or (mental n2 illness) or (mental n2 wellbeing) or (mental n2 disorder*) or (psychological n2 adjustment) or (emotional n2 adjustment) or (adjustment n2 disorder) or (emotional n2 adaptation))
3	S1 OR S2
4	MH (MH "Defibrillators, Implantable")
5	TI (((Implantable cardioverter defibrillator or ((implantable or internal or automatic or automated) n2 (cardioverter or defibrillator)) or AICD or ICD).)) OR AB (((Implantable cardioverter defibrillator or ((implantable or internal or automatic or automated) n2 (cardioverter or defibrillator)) or AICD or ICD).))
6	S4 OR S5
7	S3 AND S6
8	Limit 7 to Date of Publication: 2014-2020 Expanders - Apply equivalent subjects Narrow by Language0: - english Search modes - Boolean/Phrase

Applied Social Sciences Index & Abstracts (ASSIA) Searched 24th of July 2020

1	su(("Anxiety" OR "Anxiety disorders" OR "Anxiety- Depression" OR "Postoperative anxiety"OR "Depression" OR "Adjustment" OR "Emotional coping" OR "Emotional disorders" OR "Emotional distress" OR "Emotional disturbance" OR "Emotional wellbeing" OR "Emotional states" OR "Psychological distress" OR "Distressed people" OR "Mental illness" OR "Psychiatric disorders" OR "Mental health" OR "Adjustment disorder" OR "Affective experiences" OR "Affective disorders" OR "Affective experiences"))
2	ti(anxi* or depress* or mood disorder* or emotion* or psych* or (mental NEAR/2 status) or (affective NEAR/2 disorder*) or (low NEAR/2 mood) or dysthymia or distress or stress or (mental NEAR/2 health) or (mental NEAR/2 illness) or (mental NEAR/2 wellbeing) or (mental NEAR/2 disorder*) or (psychological NEAR/2 adjustment) or (emotional NEAR/2 adjustment) or (adjustment NEAR/2 disorder) or (emotional NEAR/2 adaptation)) OR ab(anxi* or depress* or mood disorder* or emotion* or psych* or (mental NEAR/2 status) or (affective NEAR/2 disorder*) or (low NEAR/2 mood) or dysthymia or distress or stress or (mental NEAR/2 health) or (mental NEAR/2 illness) or (mental NEAR/2 wellbeing) or (mental NEAR/2 disorder*) or (psychological NEAR/2 adjustment) or (emotional NEAR/2 adjustment) or (adjustment NEAR/2 disorder) or (emotional NEAR/2 adaptation))
3	su(("Anxiety" OR "Anxiety disorders" OR "Anxiety- Depression" OR "Postoperative anxiety" OR "Depression" OR "Adjustment" OR "Emotional coping" OR "Emotional disorders" OR "Emotional distress" OR "Emotional disturbance" OR "Emotional wellbeing" OR "Emotional states" OR "Psychological distress" OR "Distressed people" OR "Mental illness" OR "Psychiatric disorders" OR "Mental health" OR "Adjustment disorder" OR "Affective experiences" OR "Affective disorders" OR "Affective experiences")) OR (ti(anxi* OR depress* OR mood disorder* OR emotion* OR psych* OR (mental NEAR/2 status) OR (affective NEAR/2 disorder*) OR (low NEAR/2 mood) OR dysthymia OR distress OR stress OR (mental NEAR/2 health) OR (mental NEAR/2 illness) OR (mental NEAR/2 wellbeing) OR (mental NEAR/2 disorder*) OR (psychological NEAR/2 adjustment) OR (emotional NEAR/2 adjustment) OR (adjustment NEAR/2 disorder) OR (emotional NEAR/2 adaptation)) OR ab(anxi* OR depress* OR mood disorder* OR emotion* OR psych* OR (mental NEAR/2 status) OR (affective NEAR/2 disorder*) OR (low NEAR/2 mood) OR dysthymia OR distress OR stress OR (mental NEAR/2 health) OR (mental NEAR/2 illness) OR (mental NEAR/2 wellbeing) OR (mental NEAR/2 disorder*) OR (psychological NEAR/2 adjustment) OR (emotional NEAR/2 adjustment) OR (adjustment NEAR/2 disorder) OR (emotional NEAR/2 adaptation)))
4	su(("Defbrillation"))
5	ti(((Implantable cardioverter defibrillator or ((implantable or internal or automatic or automated) NEAR/2 (cardioverter or defibrillator)) or AICD or ICD).)) OR ab(((Implantable cardioverter defibrillator or ((implantable or internal or automatic or automated) NEAR/2 (cardioverter or defibrillator)) or AICD or ICD).))
6	su(("Defibrillation")) OR (ti(((Implantable cardioverter defibrillator OR ((implantable OR internal OR automatic OR automated) NEAR/2 (cardioverter OR defibrillator)) OR AICD OR ICD) .)) OR ab(((Implantable cardioverter defibrillator OR ((implantable OR internal OR automatic OR automated) NEAR/2 (cardioverter OR defibrillator)) OR AICD OR ICD) .)))

7	(su(("Anxiety" OR "Anxiety disorders" OR "Anxiety- Depression" OR "Postoperative anxiety" OR "Depression" OR "Adjustment" OR "Emotional coping" OR "Emotional disorders" OR "Emotional distress" OR "Emotional disturbance" OR "Emotional wellbeing" OR "Emotional states" OR "Psychological distress" OR "Distressed people" OR "Mental illness" OR "Psychiatric disorders" OR "Mental health" OR "Adjustment disorder" OR "Affective experiences" OR "Affective disorders" OR "Affective experiences")) OR (ti(anxi* OR depress* OR mood disorder* OR emotion* OR psych* OR (mental NEAR/2 status) OR (affective NEAR/2 disorder*) OR (low NEAR/2 mood) OR dysthymia OR distress OR stress OR (mental NEAR/2 health) OR (mental NEAR/2 illness) OR (mental NEAR/2 wellbeing) OR (mental NEAR/2 disorder*) OR (psychological NEAR/2 adjustment) OR (emotional NEAR/2 adjustment) OR (adjustment NEAR/2 disorder) OR (emotional NEAR/2 adaptation)) OR ab(anxi* OR depress* OR mood disorder* OR emotion* OR psych* OR (mental NEAR/2 status) OR (affective NEAR/2 disorder*) OR (low NEAR/2 mood) OR dysthymia OR distress OR stress OR (mental NEAR/2 health) OR (mental NEAR/2 illness) OR (mental NEAR/2 wellbeing) OR (mental NEAR/2 disorder*) OR (psychological NEAR/2 adjustment) OR (emotional NEAR/2 adjustment) OR (adjustment NEAR/2 disorder) OR (emotional NEAR/2 adaptation)))) AND (su(("Defibrillation")) OR (ti(((Implantable cardioverter defibrillator OR ((implantable OR internal OR automatic OR automated) NEAR/2 (cardioverter OR defibrillator)) OR AICD OR ICD) .)) OR ab(((Implantable cardioverter defibrillator OR ((implantable OR internal OR automatic OR automated) NEAR/2 (cardioverter OR defibrillator)) OR AICD OR ICD) .))))
8	(su(("Anxiety" OR "Anxiety disorders" OR "Anxiety- Depression" OR "Postoperative anxiety" OR "Depression" OR "Adjustment" OR "Emotional coping" OR "Emotional disorders" OR "Emotional distress" OR "Emotional disturbance" OR "Emotional wellbeing" OR "Emotional states" OR "Psychological distress" OR "Distressed people" OR "Mental illness" OR "Psychiatric disorders" OR "Mental health" OR "Adjustment disorder" OR "Affective experiences" OR "Affective disorders" OR "Affective experiences")) OR (ti(anxi* OR depress* OR mood disorder* OR emotion* OR psych* OR (mental NEAR/2 status) OR (affective NEAR/2 disorder*) OR (low NEAR/2 mood) OR dysthymia OR distress OR stress OR (mental NEAR/2 health) OR (mental NEAR/2 illness) OR (mental NEAR/2 wellbeing) OR (mental NEAR/2 disorder*) OR (psychological NEAR/2 adjustment) OR (emotional NEAR/2 adjustment) OR (adjustment NEAR/2 disorder) OR (emotional NEAR/2 adaptation)) OR ab(anxi* OR depress* OR mood disorder* OR emotion* OR psych* OR (mental NEAR/2 status) OR (affective NEAR/2 disorder*) OR (low NEAR/2 mood) OR dysthymia OR distress OR stress OR (mental NEAR/2 health) OR (mental NEAR/2 illness) OR (mental NEAR/2 wellbeing) OR (mental NEAR/2 disorder*) OR (psychological NEAR/2 adjustment) OR (emotional NEAR/2 adjustment) OR (adjustment NEAR/2 disorder) OR (emotional NEAR/2 adaptation)))) AND (su(("Defibrillation")) OR (ti(((Implantable cardioverter defibrillator OR ((implantable OR internal OR automatic OR automated) NEAR/2 (cardioverter OR defibrillator)) OR AICD OR ICD) .)) OR ab(((Implantable cardioverter defibrillator OR ((implantable OR internal OR automatic OR automated) NEAR/2 (cardioverter OR defibrillator)) OR AICD OR ICD) .)))) AND pd(2014-2020)

PsycINFO Searched 24th of July 2020

1	DE "Adjustment Disorders" OR DE "Stress" OR DE "Mental Disorders due to General Medical Conditions" OR DE "Mental Health and Illness Assessment" OR DE "Psychopathology" OR DE "Emotional and Behavioral Disorders" OR DE "Anxiety Disorders" OR DE "Emotional Assessment" OR DE "Stress and Coping Measures" OR DE "Anxiety" OR DE "Anxiety Disorders" OR DE "Neurosis" OR DE "Stress Reactions" OR DE "Emotional Adjustment" OR DE "Distress" OR DE "Major Depression" OR DE "Mental Disorders" OR DE "Psychosocial Readjustment" OR DE "Reactive Depression" OR DE "Adjustment" OR DE "Psychological Stress" OR DE "Disorders" OR DE "Affective Disorders" OR DE "Psychological Consequence" OR DE "Adaptation"
2	TI (anxi* or depress* or mood disorder* or emotion* or psych* or (mental n2 status) or (affective n2 disorder*) or (low n2 mood) or dysthymia or distress or stress or (mental n2 health) or (mental n2 illness) or (mental n2 wellbeing) or (mental n2 disorder*) or (psychological n2 adjustment) or (emotional n2 adjustment) or (adjustment n2 disorder) or (emotional n2 adaptation)) OR AB (anxi* or depress* or mood disorder* or emotion* or psych* or (mental n2 status) or (affective n2 disorder*) or (low n2 mood) or dysthymia or distress or stress or (mental n2 health) or (mental n2 illness) or (mental n2 wellbeing) or (mental n2 disorder*) or (psychological n2 adjustment) or (emotional n2 adjustment) or (adjustment n2 disorder) or (emotional n2 adaptation))
3	S1 OR S2
4	DE "Medical Therapeutic Devices"
5	TI (((Implantable cardioverter defibrillator or ((implantable or internal or automatic or automated) n2 (cardioverter or defibrillator)) or AICD or ICD).)) OR AB (((Implantable cardioverter defibrillator or ((implantable or internal or automatic or automated) n2 (cardioverter or defibrillator)) or AICD or ICD).))
6	S4 OR S5
7	S3 AND S6 : **Limiters** - Publication Year: 2014-2020, English Language **Expanders** - Apply equivalent subjects **Search modes** - Boolean/Phrase

EMBASE
Searched 24th of July 2020

1	anxiety/
2	anxiety disorder/
3	"mixed anxiety and depression"/
4	depression/
5	chronic depression/
6	major depression/
7	reactive depression/
8	minor depression/
9	postoperative depression/
10	mood disorder/
11	dysthymia/
12	psychological adjustment/
13	psychological well-being/
14	emotional stress/
15	stress/
16	adjustment disorder/

17	(anxi* or depress* or mood disorder* or emotion* or psych* or (mental adj2 status) or (affective adj2 disorder*) or (low adj2 mood) or dysthymia or distress or stress or (mental adj2 health) or (mental adj2 illness) or (mental adj2 wellbeing) or (mental adj disorder*) or (psychological adj2 adjustment) or (emotional adj2 adjustment) or (adjustment adj2 disorder) or (emotional adj2 adaptation)).ti. or (anxi* or depress* or mood disorder* or emotion* or psych* or (mental adj2 status) or (affective adj2 disorder*) or (low adj2 mood) or dysthymia or distress or stress or (mental adj2 health) or (mental adj2 illness) or (mental adj2 wellbeing) or (mental adj disorder*) or (psychological adj2 adjustment) or (emotional adj2 adjustment) or (adjustment adj2 disorder) or (emotional adj2 adaptation)).ab.
18	or/1-17
19	implantable cardioverter defibrillator/
20	(((((Implantable cardioverter defibrillator adj2 ICD) or automated implantable cardioverter defibrillator) adj2 AICD) or Automatic Implantable cardioverter defibrillator) adj2 AICD).ti. or (((((Implantable cardioverter defibrillator adj2 ICD) or automated implantable cardioverter defibrillator) adj2 AICD) or Automatic Implantable cardioverter defibrillator) adj2 AICD). ab.
21	or/19-20
22	18 and 21
23	limit 23 to English language and yr="2014 -Current")

Appendix 1.3 Electronic Search Results

Database	Interface	Limits applied	Number of Results	Date of final search
PsycINFO	EBSCOhost	English Language Year: 2014-2020	602	24/7/2020
CINAHL	EBSCOhost	English Language Year: 2014-2020	566	24/7/2020
MEDLINE	EBSCOhost	English Language Year: 2014-2020	1067	24/7/2020
Applied Social Science Index and Abstract	ProQuest	English Language Year: 2014-2020	316	24/7/2020
Psychology and Behavioral Sciences Collection	EBSCOhost	English Language Year: 2014-2020	119	24/7/2020
EMBASE	OVID	English Language Year: 2014-2020	3489	24/7/2020

Appendix 1.4 Data Extraction Form (Modified from the JBI data extraction form)

Article Title:

Authors (year):

Journal, volume (issue) and page number

Aim/objectives of the study:

Study design	
Setting/ participant characteristics	
Inclusion criteria	
Exclusion criteria	
Sample size	
Interventions	
Instrumentation	
Withdrawals/drop outs	

Results

Data

Outcomes	Group A	Group B	Group C

Authors' conclusions

Reviewer's comments

Appendix 1.5 – CCAT Quality Appraisal Tool

Crowe Critical Appraisal Tool (CCAT) Form (v1.4) Reference Reviewer

This form must be used in conjunction with the CCAT User Guide (v1.4); otherwise validity and reliability may be severely compromised.

Citation

	Year

Research design (add if not listed)

❑ Not research		Article | Editorial | Report | Opinion | Guideline | Pamphlet | …
❑ Historical		…
❑ Qualitative		Narrative | Phenomenology | Ethnography | Grounded theory | Narrative case study | …
❑ Descriptive, Exploratory, Observational		A. Cross-sectional | Longitudinal | Retrospective | Prospective | Correlational | Predictive | …
		B. Cohort | Case-control | Survey | Developmental | Normative | Case study | …
Experimental	❑ True experiment	Pre-test/post-test control group | Solomon four-group | Post-test only control group | Randomised two-factor | Placebo controlled trial | …
	❑ Quasi-experiment	Post-test only | Non-equivalent control group | Counter balanced *(cross-over)* | Multiple time series | Separate sample pre-test post-test [no Control] [Control] | …
	❑ Single system	One-shot experimental *(case study)* | Simple time series | One group pre-test/post-test | Interactive | Multiple baseline | Within subjects *(Equivalent time, repeated measures, multiple treatment)* | …
❑ Mixed Methods		Action research | Sequential | Concurrent | Transformative | …
❑ Synthesis		Systematic review | Critical review | Thematic synthesis | Meta-ethnography | Narrative synthesis | …
❑ Other		…

Variables and analysis

Intervention(s), Treatment(s), Exposure(s)	Outcome(s), Output(s), Predictor(s), Measure(s)	Data analysis method(s)

Sampling

Total size		Group 1		Group 2		Group 3		Group 4		Control	
Population, sample, setting											

Data collection (add if not listed)

Audit/Review	a) Primary | Secondary | … b) Authoritative | Partisan | Antagonist | … c) Literature | Systematic | …	Interview	a) Formal | Informal | … b) Structured | Semi-structured | Unstructured | … c) One-on-one | Group | Multiple | Self-administered | …
Observation	a) Participant | Non-participant | … b) Structured | Semi-structured | Unstructured | … c) Covert | Candid | …	Testing	a) Standardised | Norm-ref | Criterion-ref | Ipsative | … b) Objective | Subjective | … c) One-on-one | Group | Self-administered | …

Scores

Preliminaries		Design		Data Collection		Results		Total [/40]	
Introduction		Sampling		Ethical Matters		Discussion		Total [%]	

General notes

Appraise research on the merits of the research design used, not against other research designs.

Category Item	Item descriptors [☑ Present; ☒ Absent; ■ Not applicable]	Description [Important information for each item]	Score [0–5]
1. Preliminaries			
Title	1. Includes study aims ❑ and design ❑		
Abstract (assess last)	1. Key information ❑ 2. Balanced ❑ and informative ❑		
Text (assess last)	1. Sufficient detail others could reproduce ❑ 2. Clear/concise writing ❑, table(s) ❑, diagram(s) ❑, figure(s) ❑		
		Preliminaries [/5]	
2. Introduction			
Background	1. Summary of current knowledge ❑ 2. Specific problem(s) addressed ❑ and reason(s) for addressing ❑		
Objective	1. Primary objective(s), hypothesis(es), or aim(s) ❑ 2. Secondary question(s) ❑		
	Is it worth continuing?	**Introduction [/5]**	
3. Design			
Research design	1. Research design(s) chosen ❑ and why ❑ 2. Suitability of research design(s) ❑		
Intervention, Treatment, Exposure	1. Intervention(s)/treatment(s)/exposure(s) chosen ❑ and why ❑ 2. Precise details of the intervention(s)/treatment(s)/exposure(s) ❑ for each group ❑ 3. Intervention(s)/treatment(s)/exposure(s) valid ❑ and reliable ❑		
Outcome, Output, Predictor, Measure	1. Outcome(s)/output(s)/predictor(s)/measure(s) chosen ❑ and why ❑ 2. Clearly define outcome(s)/output(s)/predictor(s)/measure(s) ❑ 3. Outcome(s)/output(s)/predictor(s)/measure(s) valid ❑ and reliable ❑		
Bias, etc	1. Potential bias ❑, confounding variables ❑, effect modifiers ❑, interactions ❑ 2. Sequence generation ❑, group allocation ❑, group balance ❑, and by whom ❑ 3. Equivalent treatment of participants/cases/groups ❑		
	Is it worth continuing?	**Design [/5]**	
4. Sampling			
Sampling method	1. Sampling method(s) chosen ❑ and why ❑ 2. Suitability of sampling method ❑		
Sample size	1. Sample size ❑, how chosen ❑, and why ❑ 2. Suitability of sample size ❑		
Sampling protocol	1. Target/actual/sample population(s): description ❑ and suitability ❑ 2. Participants/cases/groups: inclusion ❑ and exclusion ❑ criteria 3. Recruitment of participants/cases/groups ❑		
	Is it worth continuing?	**Sampling [/5]**	
5. Data collection			
Collection method	1. Collection method(s) chosen ❑ and why ❑ 2. Suitability of collection method(s) ❑		
Collection protocol	1. Include date(s) ❑, location(s) ❑, setting(s) ❑, personnel ❑, materials ❑, processes ❑ 2. Method(s) to ensure/enhance quality of measurement/instrumentation ❑ 3. Manage non-participation ❑, withdrawal ❑, incomplete/lost data ❑		
	Is it worth continuing?	**Data collection [/5]**	
6. Ethical matters			
Participant ethics	1. Informed consent ❑, equity ❑ 2. Privacy ❑, confidentiality/anonymity ❑		
Researcher ethics	1. Ethical approval ❑, funding ❑, conflict(s) of interest ❑ 2. Subjectivities ❑, relationship(s) with participants/cases ❑		
	Is it worth continuing?	**Ethical matters [/5]**	
7. Results			
Analysis, Integration, Interpretation method	1. A.I.I. method(s) for primary outcome(s)/output(s)/predictor(s) chosen ❑ and why ❑ 2. Additional A.I.I. methods (e.g. subgroup analysis) chosen ❑ and why ❑ 3. Suitability of analysis/integration/interpretation method(s) ❑		
Essential analysis	1. Flow of participants/cases/groups through each stage of research ❑ 2. Demographic and other characteristics of participants/cases/groups ❑ 3. Analyse raw data ❑, response rate ❑, non-participation/withdrawal/incomplete/lost data ❑		
Outcome, Output, Predictor analysis	1. Summary of results ❑ and precision ❑ for each outcome/output/predictor/measure 2. Consideration of benefits/harms ❑, unexpected results ❑, problems/failures ❑ 3. Description of outlying data (e.g. diverse cases, adverse effects, minor themes) ❑		
		Results [/5]	
8. Discussion			
Interpretation	1. Interpretation of results in the context of current evidence ❑ and objectives ❑ 2. Draw inferences consistent with the strength of the data ❑ 3. Consideration of alternative explanations for observed results ❑ 4. Account for bias ❑, confounding/effect modifiers/interactions/imprecision ❑		
Generalisation	1. Consideration of overall practical usefulness of the study ❑ 2. Description of generalisability (external validity) of the study ❑		
Concluding remarks	1. Highlight study's particular strengths ❑ 2. Suggest steps that may improve future results (e.g. limitations) ❑ 3. Suggest further studies ❑		
		Discussion [/5]	
9. Total			
Total score	1. Add all scores for categories 1–8		
		Total [/40]	

Appendix 1.6 CCAT Quality Ratings

Author/Year	Preliminaries	Introduction	Design	Sampling	Data collection	Ethics	Results	Discussion	Total score (%)	Descriptive
1.Amiaz et al., 2016	3/5	4/5	2/5	2/5	3/5	2/5	2/5	3/5	20/40(53%)	Moderate
2.Amiaz et al., 2017	4/5	4/5	4/5	2/5	2/5	2/5	3/5	4/5	25/40(63%)	Moderate
3.Farahani et al., 2016	2/5	3/5	2/5	3/5	2/5	2/5	2/5	2/5	18/40(45%)	Low
4.Habibović, et al., 2017b	4/5	4/5	3/5	3/5	3/5	3/5	2/5	4/5	26/40(65%)	Moderate
5. Habibović et al., 2018	4/5	5/5	3/5	3/5	4/5	3/5	2/5	4/5	27/40(70%)	Moderate
6. Ichikura et al., 2017	4/5	5/5	2/5	3/5	3/5	2/5	2/5	3/5	24/40(60%)	Moderate
7.Israelsson et al., 2018	4/5	3/5	2/5	3/5	3/5	2/5	3/5	3/5	23/40(58%)	Moderate
8. Lee et al., 2020	4/5	4/5	2/5	2/5	3/5	3/5	3/5	4/5	25/40(63%)	Moderate
9. Miller, Thylén & Moser 2016	4/5	4/5	2/5	3/5	3/5	2/5	3/5	4/5	25/40(63%)	Moderate
10. Pedersen et al., 2018	3/5	4/5	3/5	3/5	4/5	3/5	2/5	3/5	25/40(63%)	Moderate

Author/Year	Preliminaries	Introduction	Design	Sampling	Data collection	Ethics	Results	Discussion	Total score	Descriptive
11.Rahmawati et al., 2016	3/5	4/5	2/5	3/5	2/5	3/5	2/5	3/5	22/40(55%)	Moderate
12. Rottmann et al., 2018	3/5	4/5	3/5	3/5	3/5	3/5	2/5	4/5	25/40(63%)	Moderate
13.Starrenburg et al., 2014	4/5	4/5	3/5	3/5	3/5	2/5	3/5	4/5	26/40(65%)	Moderate
14. Thylén et al., 2014	4/5	5/5	2/5	3/5	3/5	3/5	3/5	4/5	27/40(68%)	Moderate
15. Thylén et al., 2016	4/5	4/5	2/5	3/5	3/5	3/5	3/5	4/5	26/40(65%)	Moderate
16. Varghese, Geller & Ohlow 2019	3/5	2/5	3/5	2/5	3/5	2/5	3/5	2/5	19/40(48%)	Low
17.Wong 2016	3/5	3/5	2/5	2/5	2/5	2/5	2/5	3/5	19/40(48%)	Low
18. Wong 2018	3/5	3/5	2/5	2/5	2/5	2/5	2/5	3/5	19/40(48%)	Low
19. Wong 2019	2/5	4/5	2/5	2/5	2/5	2/5	2/5	3/5	19/40(48%)	Low

Appendix 2.1 Original Major Research Proposal (MRP) V2

Doctorate in Clinical Psychology Submission Front page

Assignment: Module 8 Major Research Project Proposal

Matriculation number:

Date of submission: 16/12/2019

Version number: 2

Word count: 3000 (excluding appendices and references)

Maximum word count: 3000 words.

Title: An Investigation into the Sociodemographic, Clinical and Psychological Variables Influencing Psychological Adjustment and Health Related Quality of Life in Implantable Cardioverter Defibrillator (ICD) Recipients.

Abstract

Background

Implantable cardioverter defibrillators (ICDs) are lifesaving devices used to treat abnormal ventricular arrhythmias. Nevertheless, a sub-set of ICD recipients experience psychological adjustment difficulties and impaired health-related quality of life (HR-QOL). Research has identified socio-demographic, clinical and psychological variables associated with distress and reduced HR-QOL among ICD recipients. However, the association of psychological flexibility (PF) with distress and HR-QOL in ICD recipients is yet to be examined.

Aims

The primary aim is to identify whether PF is associated with distress and HR-QOL in ICD recipients to determine if Acceptance and Commitment Therapy could be an indicated treatment for this population. The secondary aim is to determine socio-demographic, clinical and psychological variables associated with psychological distress and reduced HR-QOL in ICD recipients.

Method

A cross-sectional correlational design is proposed, with data being collected from ICD recipients' post-implantation. Participants will be recruited from multiple NHS clinics and using online and postal survey methods. Data on clinical, socio-demographic and psychological factors will be incorporated into a paper-based and online self-report questionnaire. Multivariate analysis is proposed.

Applications

Exploring the factors associated with distress and HR-QOL in ICD recipients may inform psychological interventions by isolating modifiable factors to be targeted in treatment.

Introduction

Implantable cardioverter defibrillators (ICDs) are used in the treatment of life-threatening ventricular arrhythmias and in the prevention of sudden cardiac death. ICDs stop ventricular arrhythmias by delivering electrical shock to restore normal heart rhythm. ICDs are indicated for individuals at risk for ventricular arrhythmia (primary prevention) or those who have survived a life-threatening ventricular arrhythmia (secondary prevention).

Benefits of ICDs are well-documented with research indicating they are more effective than pharmacological therapy at preventing sudden cardiac death (Ezekowitz, Armstrong & McAlister, 2003). The ICD is accepted by most patients; however, approximately 25-33% experience psychological adjustment difficulties and impaired HR-QOL (Pedersen et al., 2005).

Factors associated with increased distress and reduced HR-QOL in ICD recipients include being female; not being in a relationship; and being younger than fifty (Kajanova, Bulava & Eisenberger, 2014). Clinical factors, including past psychotropic medication use and the reason for ICD implant (primary versus secondary prevention), are risk factors for poorer adjustment (Kajanova, Bulava & Eisenberger, 2014). Primary prevention ICD recipients have reported heightened anxiety and reduced HR-QOL compared to secondary prevention patients (Rahmawati et al., 2016). It is hypothesised secondary prevention recipients appraise their risk of cardiac death as higher due to previous experience and therefore view their ICDs as lifesaving. Conversely, primary prevention patients have not experienced life-threatening cardiac event(s) and therefore may struggle to accept why they need the ICD.

Other clinical variables, including the number of device shocks received are associated with increased distress and reduced HR-QOL (Pedersen et al., 2005). The experience of device shock can be distressing, and the physical sensations caused by the discharge have been likened to a kick in the chest. This experience can lead to a conditioned response marked by avoidance of activities associated with ICD shock, fuelled by anticipatory anxiety of receiving shocks (Sears & Conti, 2002).

The time since ICD implantation is also associated with adjustment, with depression and anxiety reducing over time. However, data on the length of the natural adjustment period are mixed. Some research indicates the 6-24 months post-implantation period as crucial for psychological adjustment (Petrowski et al., 2013) while other research reports difficulties resolve within the first few months post-implant (Kajanova, Bulava & Eisenberger, 2014). Consensus as to the length of the adjustment period will not be determined until prospective studies of psychological outcomes in ICD patients are conducted.

Psychological explanations have been posed for patient variations in post-implant psychological adjustment. According to the Self-Regulation Model, adaptation to a health condition is an intricate self-regulation process (Leventhal, Meyer & Nerenz, 1980). Researchers hypothesise individuals develop cognitive illness representations, which assist them to understand their condition (Leventhal, Meyer & Nerenz, 1980). Using these representations, individuals develop coping responses to manage their condition.

In ICD recipients, illness perceptions including lower perceived control of health status are associated with increased distress and reduced HR-QOL (Hammash et al., 2018). Additional research has identified ICD-specific psychological factors which predict maladjustment. For example, ICD-related concerns (worry about the ICD discharging) is an independent determinant of distress after controlling for the number of shocks received (Pedersen et al., 2005).

Perceptions of control and ICD-related concerns have implications for the design of psychological interventions. For example, CBT-based treatments can promote adaptive illness perceptions. Alternatively, change can be achieved by enabling individuals to 'let go' of the notion that everything is controllable, through acceptance-based interventions (Aujoulat et al., 2008). Acceptance-based strategies may be useful for ICD recipients given device shocks are uncontrollable.

Acceptance-Based Approaches

Acceptance strategies are components of interventions including Acceptance and Commitment Therapy (ACT). Acceptance-based interventions have advantages over other models in the context of chronic physical health conditions because illness perceptions including perceived control may be realistic in conditions where recovery is not possible (Angiola & Bowen, 2013). In ACT, the proposed mechanism of change is Psychological Flexibility (PF) which is conceptualised as being "mindful of experiences in the present moment, in an accepting and non-judgmental way, while behaving consistently with one's values, even when one's thoughts and feelings oppose taking valued actions" (Levin et al., 2014, p. 21).

Targeting levels of PF may be of utility in ICD patients. Some ICD recipients avoid daily activities due to fear of receiving device shock (McCaig et al., 2014). Avoidance of valued activities relates to adjustment and remaining active despite health difficulties is recommended for well-being. ACT aims to foster PF, and to engage with valued actions in the face of distressing thoughts/feelings, which may be a useful strategy to target ICD-related avoidance patterns.

No research was identified investigating PF in ICD recipients. Research has investigated PF in other health conditions, with higher levels of PF predicting lower levels of anxiety in those with cancer (Montiel et al., 2016) and ACT being efficacious for people with chronic pain (Hann & McCracken, 2014).

Aims

The primary aim is to determine whether PF is associated with distress and HR-QOL in ICD recipients to identify whether ACT could be an indicated treatment for this population. The secondary aim is to identify the socio-demographic, clinical and psychological variables associated with distress and HR-QOL in ICD recipients.

Hypotheses:

H_1 Lower PF will be associated with greater psychological distress and reduced HR-QOL in ICD recipients.

H_2 Socio-demographic variables (younger age >50, female sex, and single marital status) will be associated with psychological distress and HR-QOL in ICD recipients.

H_3 Clinical variables (number of shocks received, ICD indication, psychotropic medication use, and time since implant) will be associated with psychological distress and HR-QOL in ICD recipients.

H_4 Psychological factors including illness perceptions (perceived control) and ICD related concerns will be associated with psychological distress and HR-QOL in ICD recipients.

H_5 ICD related concerns will be independently associated with psychological distress in ICD recipients after controlling for clinical variables mentioned in H_3.

Plan of Investigation

Participants

ICD recipients will be recruited from NHS sites including Glasgow Royal Infirmary, Queen Elizabeth, Golden Jubilee Hospital and at clinics within the NHS Ayrshire & Arran board area.

Inclusion Criteria

- Individuals >18 years old.
- Patients who have had an ICD implanted due to experiencing arrhythmias or heart failure.
- Patients who have had their ICD >2 months.
- Sufficient command of the English language to give consent and meaningfully participate.

Exclusion Criteria

- Individuals unable to complete the study due to experiencing significant cognitive impairment (Dementia, Learning Disability).
- Individuals on the waiting list for heart transplantation.
- Individuals with anoxic brain injury following events including cardiac arrest.

Recruitment & Research Procedures

Participants will be recruited by the principal researcher or cardio-physiologists at post-implantation clinics. Those who meet eligibility criteria and provide informed consent will be asked to complete paper-based questionnaires or an online response using the NHS GGC survey tool: Webropol. It is estimated 40 ICD-recipients per week attend follow-up at Glasgow Royal Infirmary and there are approximately 180 patients attending clinics within NHS Ayrshire and Arran.

Permission will also be sought to identify participants from an ICD-implant patient database stored at the Golden Jubilee Hospital. This database contains patients name, CHI number and date of ICD implantation. It is proposed the lead clinician will facilitate access to this database because they are part of the clinical team. The lead clinician will then obtain patients address details by entering individuals CHI number into electronic record systems. The principle researcher will print out packs containing participant information sheets, consent forms, and paper-based questionnaires with only members of the clinical team attaching patients address details to the packs.

Participants will then be mailed a study information sheet, information on inclusion/exclusion criteria, consent form, paper copies of questionnaires and a survey link to access online version of the survey. Participants completing the online survey, will be asked to indicate whether they have any of the conditions outlined in the exclusion criteria. If participants meet exclusion criteria they will be screened out of the survey and thanked for their interest.

Participants choosing to complete paper-based questionnaires will be asked to withdraw if they have any of the conditions mentioned in the exclusion criteria. Participants will be provided with a pre-paid envelope to enable them to return their consent forms and completed paper-questionnaires. Previous research recruiting ICD recipients via postal methods found response rates of 55% (Thylen et al., 2014).

Measures

Socio-demographic/Clinical Variables

Socio-demographic information including sex, age, marital status and educational level will be collected by self-report. Clinical variables including time since implant, number of shocks experienced, information on primary vs secondary indication for ICD-implantation, heart failure or fibrillation diagnosis and past/current psychotropic medication use will be collected by self-report.

Psychological Distress

Psychological distress will be measured with the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983). The HADS contains 14-items, 7 of which measure depression (HADS-D), and 7 measure anxiety (HADS-A). Items are scored on a 4-point Likert scale. Scores range from 0 to 3, with a total score of 0–21 for each subscale. Research suggests employing a cut-point of > 8 for each of the constituent subscales, to indicate probable caseness. This cut-off provides sensitivity and specificity of 0.80 (Bjelland et al., 2002). The Cronbach's alpha values are 0.83 and 0.82 for the HADS-A and HADS-D respectively, indicating the HADS is reliable.

HR-QOL

The EuroQol-5D-3 level (EQ-5D-3L) assesses five domains of HR-QOL: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (EuroQol Group, 1990). Items are scored on a three-point scale, ranging from 1 (no problems) to 3 (severe problems). There is a total of 243 health status combinations, each of which are referred to using a five-digit code, using the numbers 1 to 3. Once established the five-digit code can be transformed into a single mean index score, with 1.0 representing full health and -0.59 indicating the lowest index. Research supports the validity and reliability of the EuroQol-5D-3L in cardiac populations (Dyer et al., 2010).

Psychological Flexibility

The Cardiovasular Disease Acceptance and Action Questionnaire (CVD-AAQ) is an adaptation of a general measure of PF, the AAQ. The CVD-AAQ measures acceptance of thoughts and feelings related to cardiovascular illness and the degree to which these internal events interfere with individuals' ability to engage in valued action. The Italian version of the CVD-AAQ indicated fair reliability with a Cronbach's alpha of 0.75 (Spatola et al., 2014).

ICD-Related Concerns

Device related concerns will be measured with the Patient ICD-related Concerns (ICDC) questionnaire (Pedersen et al., 2005). The ICDC contains 8-items that are rated on a 5-point Likert scale from 0 (not at all) to 4 (very much so). Scores range from 0 to 32, with higher scores indicating more ICD-related concerns. There is no standardised cut-off for the ICDC; however, research propose dividing patients into a low versus high concern group, using the cut-off of >13 to indicate high concerns (Pedersen et al., 2005). The internal consistency of the ICDC is good with a Cronbach's alpha of 0.91.

Illness Perceptions

The Brief Illness Perception Questionnaire (B-IPQ) measures illness perceptions (Broadbent et al., 2006). The B-IPQ contains 9-items and is rated on a 0-10 Likert scale, which assesses cognitive illness perceptions, emotional (illness concerns), illness comprehensibility and causal representations. Scores range from 0 to 80, with a higher score reflecting a more threatening view of illness. Correlation coefficients of items in a test of test-retest reliability were $r = .88$ in a sample of cardiac patients (Rakhshan, Hassani & Ashktorab, 2011).

Design

A cross-sectional correlational design is proposed. Data will be collected from ICD recipients at one time point (post-implantation).

Data Analysis

Descriptive statistics will be calculated to summarise the independent variables (clinical, psychological and socio-demographic characteristics) and the outcome variables (HADS and Euro-QOL scores).

Univariate analyses between the independent and outcome variables will be assessed using Pearson's correlation co-efficient or independent sample t-tests depending on the level of measurement of the variables, in determining candidate explanatory variables for regression analysis.

Linear multiple regression will be used to test hypothesis 1, 2, 3 and 4 by identifying what independent variables are predictors of distress and HR-QOL.

Hierarchical regression analysis will be used to test hypothesis 5 to determine whether ICD related concerns are independently associated with symptoms of anxiety/depression despite controlling for clinical and socio-demographic variables.

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Sample Size

Recommendations for conducting regression analysis stipulates a sample of 10-15 participants per predictor. Prior research investigating whether PF is associated with distress in ICD-recipients was not identified. Nevertheless, research has reported PF predicted levels of anxiety and depression in a sample of individuals with cancer, with moderate effect sizes (r^2 = .43) (Montiel et al., 2016). G* Power was used to estimate sample size and indicated a required sample of 47 participants to conduct multiple regression based on a moderate predicted effect size ($f^2 = 0.75$), with 12 predictors ($\alpha = 0.05, \beta = 0.95$).

However, research investigating variables including the relationship between ICD-related concerns and HR-QOL have reported small effect sizes ($r^2 = .093$) (Thylén et al., 2014). Based on a small predicted effect size ($f^2 = .1$), G* Power indicated a required sample of 185 to conduct multiple regression, with 12 predictors ($\alpha = 0.05, \beta = 0.80$). Accordingly, the study will aim to recruit 185 participants.

Settings and Equipment

Data collection will occur in clinic-based settings, with participants completing measures in waiting areas or a private room if available. Required equipment includes paper copies of the questionnaires, access to the Webropol survey tool, and a secure cabinet and or encrypted laptop/computer to store data and record participants responses if completing the online survey. Other equipment includes SPSS and printing/photocopying facilities.

Health and Safety Issues

The researcher will observe the recruitment sites' health and safety procedures. The research will not involve making diagnosis of mental health problems. Nevertheless, participants will be sign-posted to their GP if they have any concerns about their physical or mental well-being. Information sheets and debrief sheets with appropriate support contact information will be provided.

Ethical Issues

Ethical Approval

The project aims to recruit NHS patients at sites including Glasgow Royal Infirmary, Queen Elizabeth University Hospital, clinics within NHS Ayrshire & Arran and from the Golden Jubilee Hospital ICD implantation database. Accordingly, an ethics application will be submitted to the NHS ethics committee and relevant NHS health boards' R&D for approval.

Informed Consent

For participants recruited at clinics, consent will be facilitated by providing individuals with an information sheet and consent form and where feasible, the study will be explained verbally by the principal researcher or cardio-physiologists. Participants will be informed their choice to decline or participate will not affect their medical care and that they have the right to withdraw. All participants will be asked if they consent to be contacted regarding future research.

For participants choosing to complete the measures using the online survey tool, the information sheet and consent form will be displayed electronically. At the end of the online survey, participants will be asked if they consent to submit their response and will be informed, they are not obliged to do so. At this stage, participants will be informed they will not be able to withdraw their data once submitted because the data will be anonymised.

For participants recruited via postal methods, consent will be indicated by their return of completed consent forms and questionnaires. All postal participants will be informed they have the right to decline the survey invitation.

Confidentiality

To ensure confidentiality, participants' responses will be anonymised and will be stored in a password protected data file. Signed consent forms will be stored in a locked cabinet separate from respondents' questionnaire responses. For participants who consent to be contacted regarding future research, their contact details will be stored in a password protected data-file on an encrypted device. Data will be stored in accordance with the Data Protection Act 2018.

Risks

Risks to participants include the identification of symptoms of anxiety/depression through their HADS scores. To ensure participants' safety, the information sheet will provide information on assessing supports by directing them to their GP and providing contact details for NHS 24, the Samaritans and Breathing Space. Additionally, for participants choosing to complete an online response a debrief page will be displayed at the end of the survey. The debrief page will encourage participants to seek a GP appointment if concerned about their well-being and provide information on supports including NHS 24 and crisis contact numbers. See appendix 1 for the health and safety form.

Financial Issues

All measures are available for use without purchase or consent has been obtained for their use. An encrypted laptop will be borrowed from University of Glasgow. Printing, photocopying and pre-paid postage costs will be incurred (See Appendix 2).

Timetable

Proposal	16th December 2019
Ethics Application	January – March 2020
Data Collection	April – October 2020
Data Analysis & Write up	November – February 2021
Final Submission	28th February 2021

Practical Applications

Identifying factors associated with distress and HR-QOL in ICD recipients could elucidate characteristics of patients at risk of developing post-implant adjustment issues. Additionally, the identification of psychological variables associated with distress can aid identification of modifiable factors to be targeted within psychological therapy. Finally, the study may be the first to investigate whether PF is associated with psychological distress and HR-QOL in ICD recipients.

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Appendix 2.2 Summary of Project Protocol

Title: Trajectories of Anxiety, Depression and Health-Related Quality of Life in Patients with Chronic Heart Failure

Lead author: Claire Davidson (Trainee Clinical Psychologist)
University Supervisors: Professor Hamish McLeod, Dr Katie Robb
Field Supervisor: Dr John Sharp
Study Type: Data Only

IRAS Reference: 291895

R&D Reference: GN20MH589

Background
Psychological adjustment to Chronic heart failure (CHF) can be challenging. A meta-analysis indicated the prevalence rate of depression was 21.5% in CHF patients, with the estimates differing depending on the use of diagnostic interview versus self-report questionnaires (19.3% and 33.6% respectively) (Rutledge et al., 2006). Additionally, a systematic review and meta-analysis reported a pool prevalence of 13.1% for anxiety disorders in people with CHF (Easton et al., 2016).

Additionally, research has shown individuals with CHF experience reduced health related quality of life (HR-QOL) compared with individuals with other health problems including chronic hemodialysis (Juenger et al., 2002). The relationship between co-occurring emotional distress in CHF patients and HR-QOL has been investigated in the literature. Individuals with depression self-report higher functional impairment and lower HR-QOL compared with people without depression and individuals with higher New York Heart Association (NYHA) severity of HF symptoms classification (Sullivan et al., 2004).

A body of research has investigated factors which predict the development of anxiety, and depression in individuals with CHF. Some data have-indicated that the development of depression appears to be associated with periods of acute worsening of HF symptoms (Johansson et al., 2013). Variance in depression and anxiety in individuals with CHF has also been associated with social-demographic factors (sex, age, socio-economic status), social factors (level/quality of social support), clinical factors (NYHA class) and psychological factors (coping styles) (Haworth et al., 2005; Lerdal et al., 2019).

Trajectories over time

Although a body of cross-sectional research has examined psychological adjustment and the associated factors/predictors in individuals with CHF, there has been limited research investigating the longitudinal trajectories of anxiety, depression and HR-QOL in patients with HF (Dekker et al., 2011; Johansson et al., 2013).

Previous HF research has indicated the severity of depression might vary or improve over time (Johansson et al., 2013). Conversely, others suggest mental health symptoms such as depression can develop following discharge from hospital (Havranek et al., 2004).

Justification

There has been limited research examining and describing the trajectories of anxiety in individuals with CHF. It is important to explore how anxiety and depression in people with CHF develops over time to identify whether anxiety/depression symptoms are transient or whether difficulties in these areas follow a more persistent course.

Aims of the study:

1. To examine the trajectories of anxiety, depression, and HR-QoL in a sample of patients with heart failure over 24-month follow-up period.

2. To explore the predictors of these trajectories, using clinical, demographic and social factors

Statistical Analysis Plan

Data Source: The proposed study will be a secondary analysis of data collected as part of a study examining palliative care needs in people with CHF (Campbell et al., 2018; REC Ref: 12/WS/0224; IRAS Ref 100839). Patients recruited into the original study consented to their anonymised data being analysed in future research. The design and rationale of the original study have been published elsewhere (Campbell et al., 2015) and involved a consecutively recruited cohort of HF patients admitted for hospital care and then followed up over 2 or 3 data collection waves. Eligible patients were aged over 18 years and met the following inclusion criteria:

Admitted to hospital (from 9th January 2013 to 1st December 2014) with a primary diagnosis of acute decompensated HF
Fulfilling the ESC diagnostic criteria for the diagnosis of HF
HF-REF, HF-PEF and valvular HF will be included.

The exclusion criteria were:
- Refusal to participate
- Unable to provide informed consent/ complete study assessments
- Confusion/ dementia
- Learning difficulties
- Unable to read or write English language
- Moribund
- Geographical reasons, not from catchment area
- Isolated cor pulmonale
- Acute coronary syndrome complicated by pulmonary oedema

All patients from the original study were eligible for inclusion in this secondary data analysis study (dependent on data completeness). The full data set is expected to comprise up to the 272 participants who were assessed in the original study.

The Robertson Centre for Biostatistics will be consulted during the execution of the statistical analysis plan. The plan for the first wave of data analysis is as follows:

Patients who provided at least one measurement of anxiety or depression (HADS) and HR-QOL measurements during the two-year follow-up period will be included in the analysis. Descriptive statistics will be run to indicate the number of patients with missing HADS and HR-QOL scores across baseline measures, and the 4, 8, 12, 16, 20- and 24-month follow-up measurements.

Patient characteristics will be summarised using means, medians, standard deviations or frequency distributions. Key descriptive statistics will be calculated for the primary outcome measures. The

standard HADS cut off point of ≥8 would be used to categorise individuals' as having clinically significant anxiety/depression symptoms at baseline and subsequent follow-up measurements.

Using an approach described in previous research (e.g., Decker et al., 2011) individuals will then be categorised into four symptom status groups based on change of HADS score or lack of significant change in HADS score from baseline to follow-up measurements:

1. No clinically significant anxiety/depression
2. Anxiety/depression improved
3. Anxiety/depression developed
4. Persistent anxiety/depression

Exploring baseline and follow-up measurements of anxiety and depression scores being using suitable regression models. This phase will involve a start and end point analysis plan. For example, the measurement between baseline (start) and one follow-up measurement (end point) will be explored at a time (e.g., at 4 months point, or 12 months (as an end point). The proposed regression analysis will adjust for, important variables.

If feasible and the data allows:

The trajectory of anxiety and depression symptoms amongst the four groups, will be analysed with repeated measures analysis of variance with Tukey honestly significant difference (HSD) post-hoc tests (following the approach of Decker et al., 2011). Nevertheless, if there is significant amount of missing data between follow-up measurements, the data will be analysed using linear mixed effects models.

Univariate analyses will also examine the relationship between each of the candidate predictor variables (e.g., symptom burden), social support access (marital status as a proxy measure) and the outcome variables (HADS score, HR-QOL scores (measured by SF-12 & Kansas Heart Failure Questionnaire). This will be assessed using Pearson's correlation co-efficient or independent sample t-tests depending on the level of measurement of the variables, in determining candidate explanatory variables for regression analysis.

Multivariate Analysis
Descriptive statistics to examine kurtosis and skew should be used to evaluate the normality of continuous outcomes prior to conducting multivariate analysis. If the data is not normal an attempt will be made to statistically transform the data. Provided assumptions are met, we will conduct Latent Class Analysis. Latent class analysis (Latent Gold) could be used to identify how many latent classes (i.e., trajectories of anxiety, depression and HR-QOL) can be described.

Data management:
Data will only be accessed and processed on the Robertson Centre for Biostatistics analytic platform via a secure remote access web portal. Data access will be restricted to Claire Davidson (the doctoral research student). All data are in anonymised form and will remain so for the purposes of analysing, interpreting and reporting the findings of this study.

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Appendix 2.3 Overview of Author's Intellectual Input into the Alternative Project

- Reviewed the heart failure literature to formulate research questions.
- Completed a project proposal and provisional statistical analysis plan.
- Screened and cleaned secondary quantitative data.
- Restructured format of data to answer the primary research questions.
- Statistical analysis – conducted statistical tests. Adapted statistical analysis plan due to missing data.
- Interpreted results from data outputs and discussed outcomes with research supervisors.
- Write-up of project.

Appendix 2.5 Table 5 and 6 Characteristics of Participants who Completed Anxiety and Depression Measures

Table 5. Characteristics of Participants Who Completed 1, 2, 3 or 4 Assessments of Anxiety

Characteristics	Participants with four anxiety measures (baseline, 4, 8 and 12-months) N = 92	Participants with three anxiety measures (baseline, 4, and 8-months) N = 37	Participants with two anxiety measures (baseline, and 4-months) N = 42	Participants with one anxiety measure (baseline only) N = 62	P value
Age	75.42 (70.37, 83.05)	76.22 (69.33, 85.12)	79.45 (73.01, 85.73)	77.39 (72.14, 82.77)	.364
Female Sex	45 (48.9%)	17 (45.9%)	21 (50.0%)	36 (58.1%)	.616
Ethnicity					.648
White	90 (97.8%)	37 (100.0%)	40 (95.2%)	60 (96.8%)	
Black	1(1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
South Asian	1 (1.1%)	0 (0.0%)	1 (2.4%)	2 (3.2%)	
Arab/Middle East	0 (0.0%)		1 (2.4%)	0 (0.0%)	
NYHA CLASS					.146
Class II	30 (32.6%)	14 (37.9%)	11 (26.2%)	13 (20.9%)	
Class III	53 (57.6%)	15 (40.5%)	21 (50.0%)	37 (59.7%)	
Class IV	9 (9.8%)	8 (21.6%)	10 (23.8%)	12 (18.4%)	
HF Symptoms					
Ankle swelling	70 (76.1%)	26 (70.3%)	32 (76.2%)	47 (75.8%)	.907
PND	62 (67.4%)	26 (70.3%)	32 (76.2%)	45 (72.6%)	.751
Orthopnea	67 (72.8%)	27 (73.0%)	31 (73.8%)	47 (75.8%)	.980
Palpitations	5 (5.4%)	1 (2.7%)	0 (0.0%)	2 (3.2%)	.521
Wheezing	24 (26.1%)	6 (16.2%)	4 (9.5%)	17 (27.4%)	.080
Baseline symptom burden score	38.00 (22.00, 51.50)	34.44 (17.78, 58.39)	39.50 (28.05, 58.50)	36.00 (16.00, 58.89)	.758
HF diagnosis prior to index admission	47 (51.1%)	9 (24.3%)	19 (45.2%)	29 (46.8%)	**.049**

Ejection Fraction < 50% >= 50%	 62(67.4%) 30 (32.6%)	 28 (75.7%) 9 (24.3%)	 34 (80.9%) 8 (19.1%)	 38 (61.3%) 24 (38.7%)	 .143
AF history	51 (55.4%)	20 (54.1%)	19 (45.2%)	36 (58.1%)	.618
MI history	39 (42.4%)	9 (24.3%)	21 (50.0%)	31 (50.0%)	.061
History of arrhythmia	7 (7.6%)	4 (10.8%)	4 (9.5%)	5 (8.1%)	.937
Current Depression	3 (3.3)	2 (5.4%)	2 (4.8%)	2 (3.2%)	.838
Depression at baseline (HADS-D ≥8)	38 (41.3%)	14 (37.8%)	18 (42.9%)	22 (36.7%)†	.906 .789
Anxiety at baseline (HADS-A ≥8)	40 (43.5%)	16 (43.2%)	22 (52.4%)	29 (46.8%)	
Depression history	12 (13.2%)†	8 (23.5%)†	5 (11.9%)†	8 (12.9%)	.570
Anti-depressant use	7 (7.6%)†	2 (5.4%)†	8 (19.1%)†	0 (0.0%)†	.099
Other Health					
Cancer	11 (12%)	1 (2.7%)	5 (11.9%)	8 (12.9%)	.392
COPD	22 (23.9%)	11 (29.7%)	7 (16.6%)	17 (27.4%)	.523
Diabetes	30 (32.6%)	7 (18.9%)	14 (33.3%)	21 (33.1%)	.394
Smoking History					.181
Current	17(18.7%)	6 (16.2%)	2 (4.8%)	9 (14.5%)	
Never smoked	56 (61.5%)	20 (54.1%)	30 (71.4%)	30 (48.4)	
Ex-smoker	18 (19.8%)	11 (29.7%)	10 (23.8%)	23 (37.1%)	
Alcohol use					.080
None	59 (64.1%)	20 (54.1%)	35 (83.3%)	44 (70.9%)	
Excess	4 (4.3%)	1 (2.7%)	2 (4.8%)	1 (1.6%)	
Previous excess	7 (7.6%)	3 (8.1%)	0 (0.0%)	1 (1.6%)	
Within recommended	22 (23.9%)	13 (35.1%)	5 (11.9%)	16 (25.8%)	

Note: Categorical variables are denoted as N and (%) Continuous variables are represented by Median and (Interquartile Range). P values were calculated using Mann Whitney U test for non-normally distributed continuous variables and the chi-square test of association for categorical variables. If the frequency in a cell was <5, p-values were calculated using Fishers exact probability test. For variables with a 2 by 2 table Yates' Correction for Continuity value is presented. ***Bolded*** *values highlight statistically significant differences. † Denotes that valid percentages are reported. Abbreviations: NYHA = New York Heart Association, HF = heart failure, AF = atrial fibrillation, MI = myocardial infarction, COPD = chronic obstructive pulmonary disease, HADS = hospital anxiety and depression scale*

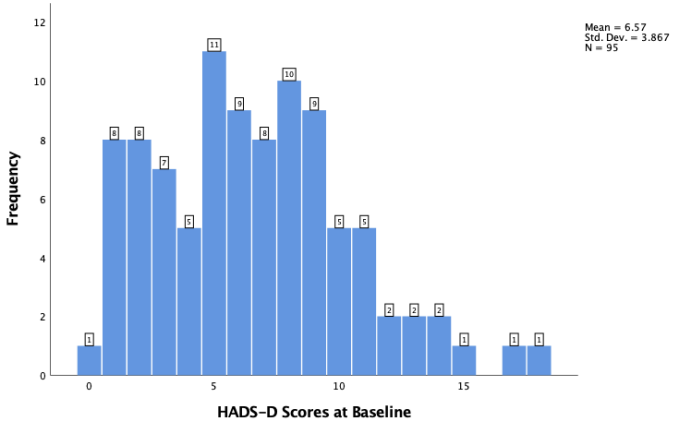
Table 6. Characteristics of Participants Who Completed 1, 2, 3 or 4 Assessments of Depression

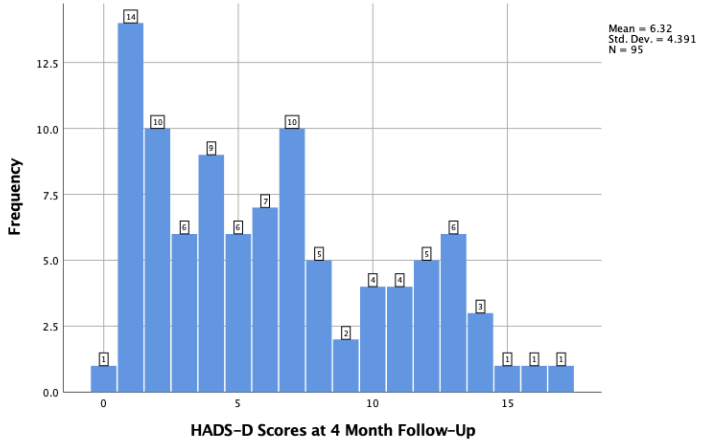
Characteristics	**Participants with four depression measures (baseline, 4, 8 and 12-months)** **N = 95**	**Participants with three depression measures (baseline, 4, and 8-months)** **N = 43**	**Participants with two depression measures (baseline, and 4-months)** **N = 43**	**Participants with one a measure (baseline only)** **N = 57**	***p* value**
Age (years)	74.35 (70.20, 82.27)	80.37 (70.90, 85.23)	79.38 (73.43, 84.15)	78.21 (72.23, 84.12)	.111
Female Sex	41 (43.2%)	22 (51.2%)	23 (53.5%)	36 (63.2%)	.121
Ethnicity					.753
White	92 (96.8%)	43 (100.0%)	41 (95.4%)	55 (96.5%)	
Black	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
South Asian	2 (2.1%)	0 (0.0%)	1 (2.3%)	2 (3.5%)	
Arab/Middle East	0 (0%)	0 (0.0%)	1 (2.3%)	0 (0.0%)	
NYHA CLASS					.051
Class II	36 (37.9%)	13 (30.2%)	11 (25.6%)	10 (17.5%)	
Class III	51 (53.7%)	20 (46.5%)	23 (53.5%)	35 (61.4%)	
Class IV	8 (8.4%)	10 (23.3%)	9 (21.0%)	12 (21.1%)	
HF Symptoms					
Ankle swelling	73 (76.8%)	32 (74.4%)	32 (74.4%)	44 (77.2%)	.978
PND	64 (67.4%)	31 (72.1%)	32 (74.4%)	41 (71.9%)	.832
Orthopnea	67 (70.5%)	32 (74.4%)	33 (76.6%)	43 (75.4%)	.851
Palpitations	3 (3.2%)	2 (4.6%)	0 (0.0%)	4 (7.0%)	.326
Wheezing	21 (22.1%)	9 (20.9%)	7 (16.3%)	18 (31.6%)	.308
Baseline symptom burden	36.00 (20.00, 50.00)	38.00 (19.00, 59.00)	43.00 (31.11, 60.00)	38.33 (18.89, 59.17)	.578
HF diagnosis prior to index	49 (51.6%)	15 (34.9%)	18 (41.9%)	24 (42.1%)	.285

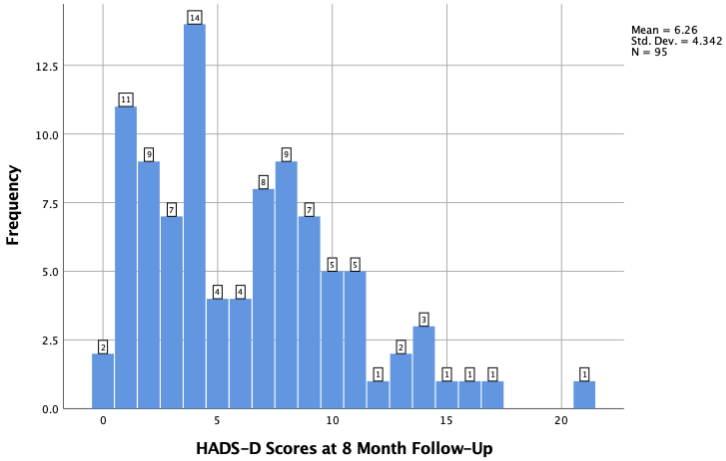
Ejection Fraction					
< 50%	64 (67.4%)	32 (74.9%)	34 (79.1%)	33 (57.9%)	.114
>= 50%	31 (32.6%)	11 (25.6%)	9 (20.9%)	24 (42.1%)	
AF history	53 (55.8%)	20 (46.5%)	20 (46.5%)	32 (56.1%)	.582
MI history	39 (41.1%)	14 (32.6)	23 (53.5%)	24 (42.1%)	.268
History of arrhythmia	8 (8.4%)	4 (9.3%)	5 (11.6%)	4 (7.0%)	.864
Current Depression	3(3.2%)†	2(4.7%)†	2 (4.7%)	3 (5.3%)	.861
Depression at baseline (HADS-D ≥8)	38 (40%)	18 (41.9%)	19 (44.2%)	21 (36.8%)	.896
Anxiety at baseline (HADS-A ≥8)	38 (40%)	21 (48.48%)	21 (50.0%)†	25 (45.5%)†	.789
Depression history	15 (15.8%)	8 (18.6%)	5 (11.6%)	7 (12.3%)	.741
Anti-depressant use	6 (6.3%)†	2 (4.7%)†	9 (20.9%)†	1 (1.8%)†	**.026**
Other Health					
Cancer	14 (14.7%)	2 (2.3%)	4 (9.3%)	6 (10.5%)	.350
COPD	22 (23.2%)	14 (32.6%)	6 (14.0%)	16 (28.1%)	.204
Diabetes	31(32.6%)	10 (23.3%)	14 (32.6%)	18 (31.6%)	.711
Smoking History					.355
Current	17(18.1%)	6 (14.0%)	3 (7.0%)	10 (17.5%)	
Never smoked	55(58.5%)	26 (60.5%)†	29 (67.4%)	29 (50.9%)	
Ex-smoker	22(23.4%)	11 (25.5%)	11 (25.6%)	18 (31.6%)	
Alcohol use					**.012**
None	61 (64.2%)	26 (60.4%)	35 (81.4%)	40 (70.2%)	
Excess	4 (4.2%)	0 (0.0%)	4 (9.3%)	0 (0.0%)	
Previous excess	6 (6.3%)	3 (7.0%)	1 (2.3%)	1 (1.8%)	
Within recommended	24 (25.3%)	14 (32.6%)	3 (7.0%)	16 (28.0%)	

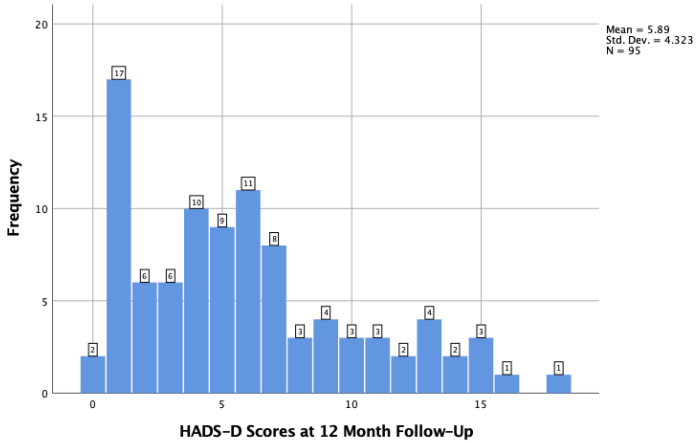
Note: Categorical variables are denoted as N and (%) Continuous variables are represented by Median and (Interquartile Range). P values were calculated using Mann Whitney U test for non-normally distributed continuous variables and the chi-square test of association for categorical variables. If the frequency in a cell was <5, p-values were calculated using Fishers exact probability test. For variables with a 2 by 2 table Yates' Correction for Continuity value is presented. ***Bolded*** *values highlight statistically significant differences. † Denotes that valid percentages are reported. Abbreviations: NYHA = New York Heart Association, HF = heart failure, AF = atrial fibrillation, MI = myocardial infarction, COPD = chronic obstructive pulmonary disease, HADS = hospital anxiety and depression scale.*

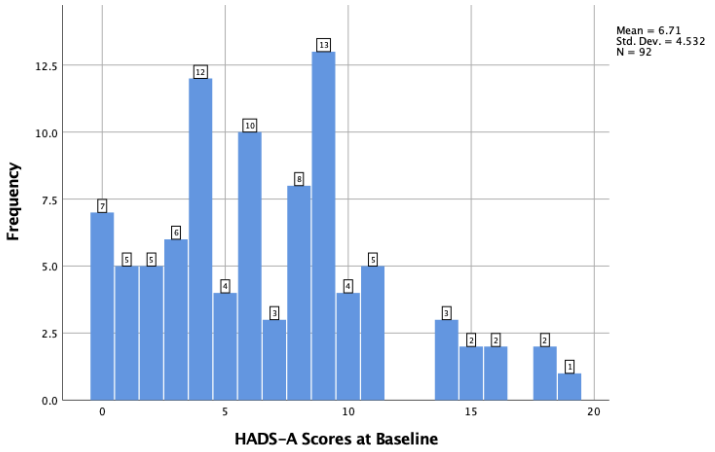
Appendix 2.6 Histograms of Participants Anxiety and Depression Scores

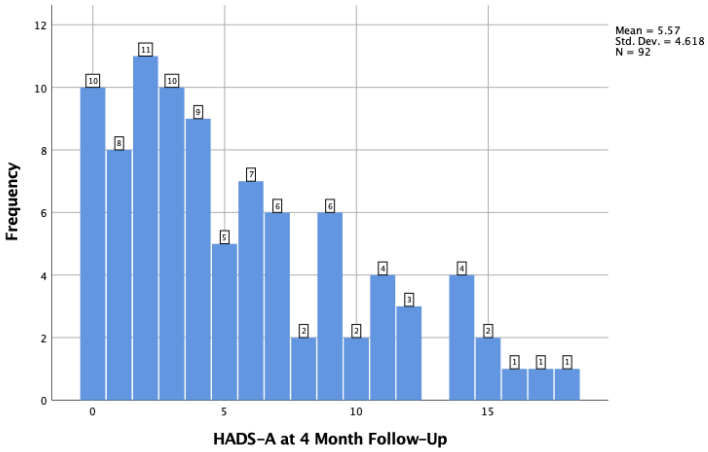


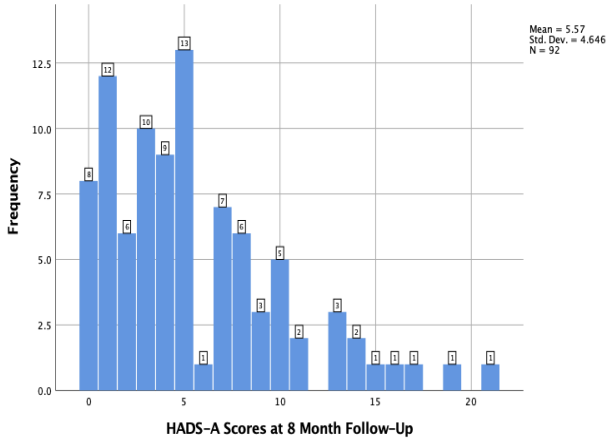


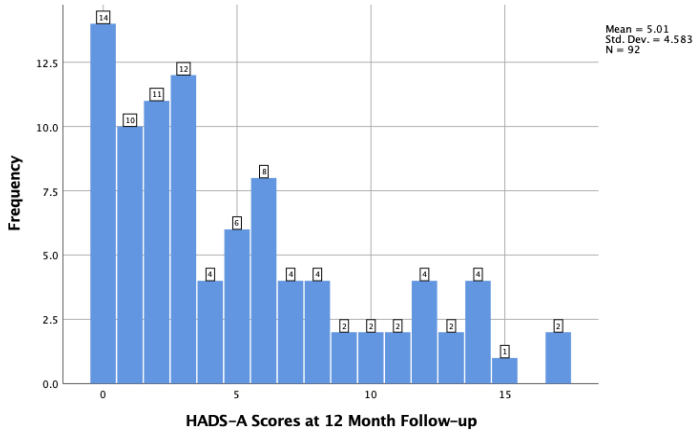





Mean = 6.71
Std. Dev. = 4.532
N = 92
Frequency
HADS-A Scores at Baseline


Mean = 5.57
Std. Dev. = 4.618
N = 92
Frequency
HADS-A at 4 Month Follow-Up


Mean = 5.57
Std. Dev. = 4.646
N = 92
Frequency
HADS-A Scores at 8 Month Follow-Up


Mean = 5.01
Std. Dev. = 4.583
N = 92
Frequency
HADS-A Scores at 12 Month Follow-up