# The Effectiveness of Cognitive Behavioural Therapy for Secondary Prevention of Coronary Heart Disease: A Meta-Analysis

by

Rebecca Kathleen Ellis

A thesis submitted in partial fulfillment of the requirements for the degree of

Master of Nursing

Faculty of Nursing
University of Alberta

**Abstract**

The effectiveness of secondary prevention (SP) for coronary heart disease (CHD) is well established. The poor integration of evidence into clinical practice remains problematic, in part due to the poor description of trials evaluating these programs. As a result, knowledge users remain unclear about which features of these SP interventions are effective for patients with CHD. The purpose was to determine the effectiveness of cognitive behavioural therapy (CBT)-based interventions for SP of CHD when compared to usual care, specialist care, or traditional cardiac rehabilitation (CR) programs. This was a systematic review of existing evidence, incorporating meta-analytic techniques. The authors searched MEDLINE (1992–2014), the EBM Cochrane Central Register of Controlled Trials, EMBASE, CINAHL, PsycINFO, and Scopus. They also contacted primary authors and hand-searched key journals, Google Scholar, and National Library of Medicine clinical trial registry (NLMCTR). An updated search of Google Scholar and NLMCTR was completed in March 2015. Two reviewers identified trials and extracted data independently; mean differences, standardized mean differences and summary risk ratios were calculated for identified outcomes using a random effects model. The authors identified 17 randomized controlled trials (RCT) (5060 patients with CHD) that met inclusion criteria. CBT-based interventions were more effective at reducing depression compared to non-CBT based CR, usual care or specialist care (11 trials, n=3133, 95% CI -0.29: -0.50 to -0.08). Multi-modality CBT-based interventions were more beneficial than specialist care alone (2 trials, n=272, 95% CI 0.27: -0.51 to -0.03), however, CBT based multi-modality interventions showed no added benefits over CR alone (3 trials, n=607, 95% CI 0.12: -0.12 to 0.35). In terms of stress reduction, CBT-based interventions were more beneficial than non-CBT based interventions (4 trials, n=642, 95% CI -1.41: -2.64 to -0.19). Finally, multiple modality CBT-based interventions

had favorable non-significant effects on morbidity (3 trials, n=572, 95% CI 0.85: 0.67 to 1.08), mortality (3 trials, n=2965, 95% CI 0.52: 0.22 to 1.23) and stress (3 trials, n=395, 95% CI -1.41: -0.31 to 0.09). All outcomes were evaluated over a mean follow up of 19.2 months (SD=27.1). Interpretations were limited by the variable quality of included trials and by the heterogeneity of reported outcomes, comparisons, and poor description of the CBT-based interventions. Conclusions are tempered by concerns around generalizability; although women were well-represented in our review, ethnicity data were generally lacking. A number of trials purposively sampled depressed patients, thus this population may be overrepresented. Conclusions were not made on cost-effectiveness due to inconsistent availability of long-term data and absence of economic outcomes. In summary, CBT-based interventions more effectively reduce depression than interventions that do not use CBT as a theoretical basis. Given the global disease burden of depression, and the poor health effects of concomitant CHD and depression, these findings have significant implications for the provision of SP for CHD. In order to facilitate translation of these key findings to clinical practice, a stronger evidence base is needed. Investigators need to thoroughly report methods to facilitate risk of bias assessment. Complex healthcare interventions must be more comprehensively described to ensure clarity of which components contributed to successes or failures. Uniform strategies for evaluation should ensure researchers are making useful comparisons to deliver useable evidence. Finally, long-term follow up is required to measure cost-effectiveness and long-term benefits of SP interventions on CHD.

## Preface

(Mandatory due to collaborative work)

A portion of the research conducted for this thesis forms part of a CIHR-funded interdisciplinary collaboration for knowledge translation, led by Professor A. M. Clark at the University of Alberta in collaboration with Professor. H. M. Arthur at McMaster University and co-investigators Oh, P., Stone, J., Briffa, T., Chambers, T., Choby, A., Neubeck, L., Redfern, J., Shiri, A. and Thirsk, L. (Clark, 2013b). The systematic review protocol in Chapter Two of this manuscript was developed by myself, with the assistance of Dr. A. M. Clark. The data synthesis in Chapter One and concluding analysis in Chapter One are my original work, as well as the literature review in Chapter One and conclusion in Chapter Five.

Chapter Three and Four of this thesis are being developed for publication; this manuscript is not yet complete nor submitted. I was responsible for the data collection, synthesis and analysis as well as drafting a manuscript. Dr. Clark assisted data synthesis, analysis and interpretation, and contributed significantly to the manuscript.

**Acknowledgements**

I wish to express my sincere gratitude to my Master's supervisor and mentor, Dr. Alex Clark. Throughout this process and my degree, Dr. Clark has stood as an exceptional example of what an academic and nurse researcher should be. Dr. Clark has provided me access to an array of resources necessary for the completion of my project, including his time and thoughtful mentorship.

I am very thankful to the members of my supervisory committee, Dr. Sandra Davidson and Dr. Dawn Kingston. Throughout my committee meetings and unscheduled discussions, they have provided me with valuable guidance and constructive criticism. In particular, I wish to sincerely thank Dr. Davidson for her wisdom, kindness, authenticity, and support – both emotional and academic – throughout my program. I am so grateful to have had such wonderful mentors.

I would like to recognize in particular Kelly Weins and Lianne Mclean. Kelly I truly appreciate your insights, support and advice. I'm so thankful to have a colleague to share this graduate and life experience with, who is as driven and realistic as Lianne.

I wish to thank my Mom, Daddy, Cara, Laura and Kerri for their unconditional love, understanding, and stability. I am so proud to say I have a successful engineer and father, wise mother and teacher, brilliant basic scientist and fellow philosopher, witty and mature kindergarten teacher, and a focused but grounded cardiac nurse in my family. A special thanks to Cara for her statistical assistance, coffee breaks and general graduate school advice.

To John, I genuinely thank you for the loving support you provide in all aspects of my life. Through all my ups and downs of this degree, including (admittedly) some grandiose delusions, you have comforted me and reminded me of what is really valuable in life and in my career.

**Abbreviations:**

| *Acronym* | *Term* |
|---|---|
| CBT | Cognitive Behavioural Therapy |
| CHD | Coronary Heart Disease |
| QOL | Quality of Life |
| RCT | Randomized Controlled Trial |
| SP | Secondary Prevention |
| CACPR | Canadian Association of Cardiovascular Prevention and Rehabilitation |
| CCS | Canadian Cardiovascular Society |
| CIHR | Canadian Institute of Health Research |
| NP | Nurse Practitioner |
| RRR | Relative risk ratio |
| RR | Risk ratio |
| NP | Nurse Practitioner |
| SMD | Standardized mean difference |
| MD | Mean difference |
| USNLM | United States National Library of Medicine |
| SBP | Systolic blood pressure |
| BMI | Body Mass Index |

**List of Tables:**

## List of Appendices:

TABLE OF CONTENTS

# The Effectiveness of Cognitive Behavioural Therapy in Secondary Prevention of Coronary Heart Disease: A Meta-Analysis

This details the processes and outcomes of a Master's thesis in the Faculty of Nursing at the University of Alberta. This thesis work involved a systematic review and meta-analysis of interventions that utilized cognitive behavioural therapy (CBT) techniques to guide secondary prevention (SP) of coronary heart disease (CHD). This manuscript details one systematic review that is a component of an ongoing larger review, titled INSPECT (INtricacies of Secondary prevention Programs for Evaluation and Control Trials) and funded by the Canadian Institute of Health Research (CIHR) (Clark et al., 2013a). A multidisciplinary team of researchers and knowledge users will utilize The INSPECT Taxonomy to classify, systematically describe and review published trials of SP programs for CHD (Clark et al., 2013b). By classifying all publications of these interventions and then identifying which components of these programs are more effective, this synthesis will add value to past research and generate specific knowledge that is accurate and useful. The sub-review detailed in this manuscript will benefit the INSPECT team's development of translatable knowledge about these pivotal factors to knowledge users locally, nationally, and internationally (Clark et al., 2013a). In Chapter One of the following document, the current state of the evidence for interventions aimed at SP of CHD is presented, identifying the background and necessity for this review; consequences of the poor clinical integration of the evidence supporting SP interventions for CHD are also addressed. Chapter Two provides the complete systematic review protocol, outlining the precise methods of implementation. Chapter Three articulates findings and data synthesis through meta-analysis. A discussion of these findings, along with implications and limitations is provided in Chapter Four.

Finally, Chapter Five concludes this manuscript by identifying the contribution that this thesis work makes for the nursing profession.

# CHAPTER ONE: BACKGROUND AND PURPOSE IN THE CONTEXT OF THE LITERATURE

### 1.1 Coronary Heart Disease

Coronary heart disease (CHD) remains a global problem (Lopez, Mathers, Ezzati, Jamison, & Murray, 2006). The Global Burden of Disease study by the World Health Organization (WHO) identified CHD and cerebrovascular disease as the leading causes of death in high, middle and low income countries, combined responsible for more than 20 percent of all deaths worldwide (Lopez et al., 2006; Mathers, Boerma, & Ma Fat, 2004). These estimates are likely to have worsened in recent years, as populations' age and risk factors become more prevalent. CHD does not only increase mortality risk, but also leads to poor quality of life (QOL). The WHO projected that by 2030, cerebrovascular disease would become a leading cause in reduction of disability-adjusted life years (DALY) (Mathers et al., 2004); DALY refers to the number of years of healthy life lost by virtue of being in states of poor health or disability (Mathers et al., 2004). In addition, more people are living longer with symptomatic CHD, requiring better access to secondary prevention (SP) health services to improve QOL; the adoption of healthy behaviours through SP strategies has the potential to reduce likelihood of premature death in people with CHD by more than double (Clark, Redfern, & Briffa, 2014; Stone, Clark, & Arena, 2009). Within Canada specifically, CHD is the leading cause of death; costs to the Canadian healthcare system are staggering; Public Health Agency of Canada data indicate that cardiovascular diseases cost the economy $22.2 billion in direct and indirect costs in 2000 (Canadian Nurses Association, 2013).

CHD in adult populations can be a broad ranging diagnosis, but for the purposes of this review we limit it to include angina, coronary artery disease and acute coronary syndromes. CHD is no longer viewed as an exclusively acute care disease. A plethora of research has clearly demonstrated the "chronic inflammatory and episodic relapsing nature of vascular disease"

(Bisoendial, Kastelein, & Stroes, 2007; Hansson, 2009; Stone et al., 2009). When viewed as a chronic disease process, CHD necessitates treatment and management as such. The Canadian Association of Cardiovascular Prevention and Rehabilitation (CACPR) guidelines identify that although early and appropriate revascularization of coronary lesions has improved short term outcomes for patients, long term advances in both quality of life and other outcomes are more dependent upon positive changes to modifiable cardiac risk factors (Stone et al., 2009). Modifiable cardiac risk factors include hypertension, dyslipidemia, obesity, tobacco use, excessive alcohol consumption, inactivity, stress and diabetes (Heart and Stroke, 2012). Patients must make healthy behaviour choices in order to prevent or minimize the progression and impact of this chronic disease. Thus, the utilization of evidence-driven secondary prevention programs which address these modifiable risk factors for CHD will more effectively "alter the progressive inflammatory nature of vascular atherosclerosis than… programs or patient services which focus principally on patient symptoms." (Stone et al., 2009).

Contemporary SP programs focus on the chronic nature of CHD. In Canada, the majority of these programs are labelled cardiac rehabilitation (CR), but vary significantly in their delivery and terminology (Clark, 2013a). For the purposes of this review, the term SP will refer to these programs in their entirety. Strategies for reducing modifiable cardiovascular risk in people with CHD are most often provided by multidisciplinary teams of health professionals. SP programs are defined in the literature as,

"*Coordinated, multifaceted interventions designed to optimize cardiac patient's physical, psychological, and social functioning, in addition to stabilizing, slowing, or even reversing the progression of the underlying atherosclerotic processes, thereby reducing morbidity and mortality*" (Taylor et al., 2004).

The most common strategies of these programs target modifiable cardiovascular risk factors, including behaviours associated with physical activity, smoking, diet and weight management, and psychosocial health. Traditionally programs may be based out of hospital or community settings and generally involve patients recruited one month after hospital discharge for two to six hours per week . Program duration is also variable, although CACPR guidelines endorse program length at least 12 weeks (Oh et al., 2009). There is consistent favourable evidence that SP programs are effective; the largest and most recent meta-analysis of 63 trials of SP interventions (21,295 patients) identified that these interventions improve all-cause mortality by 15% (95% CI: 0.77 to 0.94), reduce risk of recurrent myocardial infarction (MI) by 17% (95% CI: 0.74 to 0.94), improve quality of life, and are associated with minimal harms (Clark, Hartling, Vandermeer, & McAlister, 2005). Though evidence of the effectiveness of SP programs for CHD is abundant, it is ostensibly unused; according to Clark et al., this wealth of evidence has had a marginal effect on access, equity, referral or outcomes in clinical practice (Clark, Redfern, Thompson, & Briffa, 2012). Part of the problem is that it remains unclear *which* interventions included in SP programs are producing the improvements in outcomes (Clark, Redfern, et al., 2012). So then, a comprehensive analysis and description of the individual components of these interventions is warranted and timely.

### 1.2 Cognitive Behavioural Therapy

One promising intervention that has been included in SP programs for CHD is cognitive behavioural therapy (CBT). CBT is a psychotherapeutic model that involves counselling through specific techniques to aid patients in modifying their habitual thinking patterns; new perspectives are created in order to elicit lasting behaviour change (Furze, Donnison, & Lewin, 2008). Dr. Robert Lewin, professor emeritus at York University, is a leading researcher on self-management

of chronic cardiac illness. Through randomized controlled trials, he has developed and validated a number of cognitive-behaviour self-management programs (University of York, 2014) and therefore his definition of CBT will be used for the purposes of this review. Lewin defines CBT as,

*"A psychotherapeutic model, the central tenet of which is that the way we think (cognition) influences our emotions and behaviour; in turn, our behaviour and emotions influence our thinking. A central task for cognitive behavioural psychotherapists is to enable clients to develop a deeper awareness of their thoughts and how these affect emotions (including associated physiological feelings) and behaviour. Clients are helped to explore the usefulness and validity of habitual ways of thinking and to develop new perspectives"* (Furze et al., 2008).

In CBT three levels of cognition are usually described: core beliefs or schemas, rules or assumptions, and automatic thoughts (Willson & Branch, 2007). The fundamental premise of CBT is that thinking, mood, physical symptoms and behaviours are all interrelated (Halford & Brown, 2009). Responses to an event are not determined strictly by the event, but also an individual's cognitive appraisal of the event (Halford & Brown, 2009). This appraisal is in turn be influenced by past experiences and other aspects of the current situation. Through becoming aware of habitual ways (and harmful) of thinking, clients can develop more constructive thought patterns, and subsequently modify undesirable behaviours (Furze et al., 2008).

The use of psychological interventions for patients with various chronic diseases is known to reduce the risk of ill health (Halford & Brown, 2009; Peyrot & Rubin, 2007). CBT has been included as a basis for many of these interventions, using self-management techniques to help patients better manage their chronic conditions (Furze et al., 2008; Halford & Brown, 2009). As

academics and practitioners are now better addressing CHD as a chronic condition (J. Stone et al., 2009), it follows that CBT may also have value in this patient population. The most recent CACPR guidelines endorse the value of psychosocial interventions for SP of CHD, as they improve patient uptake and adherence to positive health behaviour interventions as well as pharmacological therapies (J. Stone et al., 2009). In fact, aspects of CBT in particular have been incorporated into some programs aimed at risk factor reduction for cardiac patients, though these have not been adequately described nor investigated (Clark et al., 2014). While CBT as an adjunctive treatment in chronic physical illness has proven effective in reducing depression and anxiety (Halford & Brown, 2009; Kunik et al., 2008; Lustman et al., 1998; Moore et al., 2007; O'Neil, Sanderson, Oldenburg, & Taylor, 2011), there is a paucity of quality evidence on its effectiveness specifically for SP of CHD. Thus, in order to provide high quality and usable evidence, and to optimize program delivery, the effectiveness of CBT specifically for CHD patients should be examined and evaluated. A systematic review of trials that evaluate the effectiveness of CBT for secondary prevention of CHD has not previously been done.

### 1.3 Problem Statement

SP programs for CHD are common throughout high-income countries, and are diverse in their components and delivery, but tend to be poorly or vaguely defined in published reports of randomized trials and systematic reviews (Glasziou et al., 2010). For example, data from the CACPR indicate that 190 formalized programs have been developed across Canada; 750 different providers exist across North America and Europe (Stone, Arthur, & Suskin, 2009). This wide array of interventions, whose components differ in a variety of ways, has implications for knowledge translation; knowledge users require consistent and accessible information in order to fund, develop, design and deliver programs to patients.

Despite thirty years of interventions studies, it was only recently that researchers in this field recognized that "complex and diverse secondary prevention programs have been inconsistently and often vaguely described" (Clark, Redfern, et al., 2012, p. 348). Poor labelling, inadequate detail of intervention components, lack of long-term figures and the inability to synthesize data on which program components most influence outcomes are all problematic (Clark et al., 2005; Clark, Redfern, et al., 2012). Although SP programs for CHD have been shown to be effective, evidence alone is not sufficient to support research utilization and knowledge translation (Clark, Redfern, et al., 2012); if ambiguously described, "program components can be conceptualized in a variety of different ways that have markedly different assumptions and implications" (Clark, 2013b). Poor description of program components prevents their replication by knowledge users involved in program planning; evidence of effectiveness of the SP programs is essentially unusable if it is not replicable (Clark, Redfern, et al., 2012). Clinicians, patients and researchers should have easy access to the information they need, else potentially effective and beneficial interventions may be used incorrectly or not at all (Glasziou et al., 2010; Mathers et al., 2004).

Poor descriptions of SP programs have two potential consequences that affect both knowledge users and patients. First, those involved in program planning at the clinical level may find the abundance of evidence in this area both overwhelming and too general and thus be unable to separate high quality evidence from extraneous information (Clark, 2013b; Clark et al., 2014). This information creates uncertainty about which program components will be most beneficial for which patients. Knowledge users subsequently have difficulty making informed decisions, and the usefulness of time consuming and costly research is compromised (Clark, 2013a; Petticrew & Roberts, 2006). As a result, these programs are underutilized by patients and prescribers alike, both nationally and internationally (Wenger, 2013).

Poor description of the components of SP programs also severely constrains the quality and usefulness of past and future research. Improved program descriptions will generate more specific, applicable knowledge for future program development and add extensive value to past research. Generating an evidence base that is practical and functional for knowledge users depends on providing specific research on what types of programs are likely to benefit which types of patients (Clark, Redfern, et al., 2012). It is therefore necessary to improve descriptions of these programs to determine common factors that lead to patient successes, with the end goal of providing excellent quality evidence for knowledge users. As earlier detailed, SP program components are complex and diverse; they occur in a wide range of settings, are provided by divers healthcare professionals, target different outcomes, have differing theoretical backgrounds and include a variety of components. CBT techniques have been used as part of SP programs for chronic disease, and although this has included CHD programs, its effectiveness has been understudied (Gulliksson et al., 2011). The goals of this review are to work concomitantly with the larger body of research to find, evaluate and describe a subset of SP programs that utilize CBT to underpin their intervention.

### 1.4 Hypothesis

The hypotheses of this project are as follows:

*Null Hypothesis:* Meta-analysis will identify no differences between CBT-based SP interventions and control groups in terms of the identified outcomes for patients with CHD when compared to usual care, specialist care, and traditional CR.

*Alternative Hypothesis:* Meta-analysis will identify a significant difference between CBT-based SP interventions and control groups in terms of the identified outcomes for patients with CHD when compared to usual care, specialist care, and traditional CR.

### 1.5 Conclusion

This secondary analysis of the evidence may be a stepping stone for future program planning and development in the area of heart disease treatment and prevention, and has the potential to improve delivery of SP to adult patients with CHD both within Canada and globally. The reduction of current costs and the future burden of CHD is paramount; specific evidence on which program components matter most is needed to ameliorate these concerns. The potential value that CBT-based interventions have is futile unless the evidence to support it is of high quality and persuasive. Thus, the evidence surrounding the effectiveness of CBT specifically for SP of CHD must be collected, analyzed, and presented systematically. It is only in this way that knowledge users, and ultimately patients, will be able to benefit from the most effective and efficient SP programs for CHD.

# CHAPTER 2: METHODOLOGY

### 2.1 Research Question

The research question for this study was developed using the PICOS tool. PICO is well established as an effective format for developing research questions for systematic reviews (CRD, 2009). This tool frames the question in terms of the population, intervention, comparator, outcome and study design; these are each central concepts germane to the following research question:

*What is the effectiveness of CBT-guided secondary prevention interventions for adult patients with coronary heart disease on primary outcomes of:*

- *Biomedical markers (blood pressure, lipid profile, body mass index, and smoking rates)*
- *Recurrent myocardial infarction (MI), all-cause mortality, hospitalization rates*
- *Psychosocial outcomes of including quality of life (QOL), anxiety, depression, stress and hostility*
- *Cost effectiveness*

*when compared to equivalent secondary prevention programs (usual care, specialist care or traditional CR)?*

By determining the effectiveness of CBT for SP in CHD patients, this synthesis will add value to past research and generate specific knowledge that is accurate and useful for knowledge users. Meta-analysis of selected studies was chosen as our method of synthesizing and evaluating the evidence, as it is well established as the most systematic way to present evidence about the effectiveness of a program or intervention (CRD, 2009). Primary aims of this review were to find, classify and evaluate previously conducted research comparing SP programs for CHD that utilize aspects of CBT to those that do not. Intentions were to identify applicable trials that meet inclusion criteria, to determine appropriate comparisons, and then evaluate each trial's CBT

intervention on overall effectiveness on the primary outcomes of hospitalization rates, biomedical markers (blood pressure, lipid profile, and body mass index), smoking rates, recurrent myocardial infarction (MI), and all-cause mortality; important psychosocial outcomes include quality of life, anxiety, depression, stress and hostility. Psychosocial risk factors are equally important as other risk factors as there is now strong, prospective evidence that psychosocial factors are associated with an increased risk of developing symptomatic coronary artery disease and convey a worse prognosis in cardiovascular populations (Prior, Francis, Reitav, & Stone, 2009), and the central tenant of CBT is thought modification to elicit behaviour change.

### 2.2 Inclusion Criteria

Criteria for inclusion in this review covered randomized controlled trial (RCT) design, which are best suited to answer the primary aims as well as the research question (Petticrew & Roberts, 2006). As the intention of this review was to determine the effectiveness of an intervention (CBT), this design is most appropriate; RCTs are rigorous and provide high quality evidence suitable for a meta-analysis. RCTs represent the most internally valid studies for answering this type of question (Petticrew & Roberts, 2006). It is important to consider that the inclusion of only RCTs does not necessarily ameliorate all concerns regarding external validity; this topic is addressed in the discussion section of this paper.

This review included trials that studied participants above the age of 18 (adults), with a diagnosis of CHD, and who were outpatients. Trials involving inpatients were excluded as they are a dissimilar patient population with diverse management needs and therefore outcome measurement differ. The diagnosis of CHD included patients with acute coronary syndromes (ACS), including ST elevation MI, Non-ST elevation MI, or angina (stable or unstable). As well,

we included patients who had documented CHD without an ACS, and post or pre-operative coronary artery bypass grafting (CABG). Trials involving patients with heart failure as their primary diagnosis were excluded as their method of care and management differs significantly (J. A. Stone et al., 2009). In addition, patients who experienced cardiac arrests were excluded, as the etiology of the cardiac arrest may be unknown and thus not CHD.

The review included trials that described an intervention that was based upon CBT principles. The use of CBT principles had to be explicit, as a diverse array of other methodologies exist to inform intervention design, but are not as robust nor evidence-based (Furze et al., 2008). Guidance on appropriate terminology for these components was gathered from members of the supervisory committee with expertise in the area of psychological interventions and cognitive behavioural therapy (D.K.). As well, interventions identified as being founded on "The Heart Manual" were included. R Lewin and colleagues developed "The Heart Manual" program centred strongly on CBT principles (Lewin, Robertson, Cay, Irving, & Campbell, 1992). Interventions based on other psychotherapies were excluded, such as hypnotherapy, interpersonal therapy, and acceptance and commitment therapy; these are designed with different foci and approaches (Furze et al., 2008). CBT differs from other theories in that it uses empirically supported techniques, is endorsed in guidelines of the National Institute for Health and Clinical Excellence, looks at how thoughts effect behaviour and aims for solid outcomes using guided discovery (Furze et al., 2008). CBT focuses on the importance of self-management, which is essential for maintenance of change in chronic illness (Willson & Branch, 2007).

Current CACPR guidelines recommend program length at least three weeks, ideally 12 weeks, with patients having therapy at a minimum frequency of once weekly; we excluded

programs that did not have contact with patients during the intervention at least once weekly. This review also did not exclude trials in which patients did not complete all therapy but were still in the intervention group, but concerns around attrition bias are presented both graphically and in the discussion section of this manuscript. Presentation in this way will account for possible attrition bias (Centre for Review and Dissemination, 2009).

In regards to classification of both in interventions and control groups, we identified a priori the importance of identifying what type of care patients were receiving. CBT-based interventions were classified as either single or multi-modality. Single modality interventions address only one cardiac risk factor, while multi-modality interventions address more than one cardiac risk factor. In control groups, any follow-up that addressed more than one cardiac risk factor was labelled traditional CR; this would include programs identified as cardiac rehabilitation or those that were multi-modality interventions that *did not* identify the use of CBT components or principles, or reference CBT as a theoretical background. Usual care was defined as any medical care that did not specifically address modification of cardiac risk factors. Specialist care included any care that included some focus on risk factor modification, without the use of CBT, but were single modality and not a formal SP program. For example, this may include follow-up with a cardiologist or cardiac nurse in addition to a general practitioner's care. In the review protocol, we intended to include only trials that evaluated a CBT-based intervention added to traditional CR, compared to a traditional CR control group. Unfortunately this was not feasible due to the small number of trials found, as well as the heterogeneity of the controls groups in these trials; this will be addressed in subsequent discussion.

Finally, measured outcomes were primarily focused on commonly reported risk factors for CHD, as well as traditional endpoints such as mortality and morbidity. In the review protocol, we

aimed to extract data about hospitalization rates, effects on individual biomedical risk factors for CHD (specifically blood pressure, lipid profile, and body mass index), recurrent MI, and all-cause mortality. Specifically important to this review were quality of life (QOL) measures such as anxiety, depression and hostility, as well as behaviour changes including smoking cessation and body mass index (BMI). We were particularly interested in differences categorized according to sex; this is a current trend in the research prescribed by the Canadian Institute of Health Research (CIHR) (CIHR, 2012). Specifically, researchers have noticed gender based differences in presentation of CHD, age at diagnosis, lifestyle factors, and referral and attendance patterns to SP programs (De Feo et al., 2012). It is important to account for these differences in order to present the best quality and most applicable evidence in this review. Of equal interest were cost-effectiveness outcomes; evidence that is intended to inform healthcare policy and guidelines must include economic measures (Clark et al., 2005).

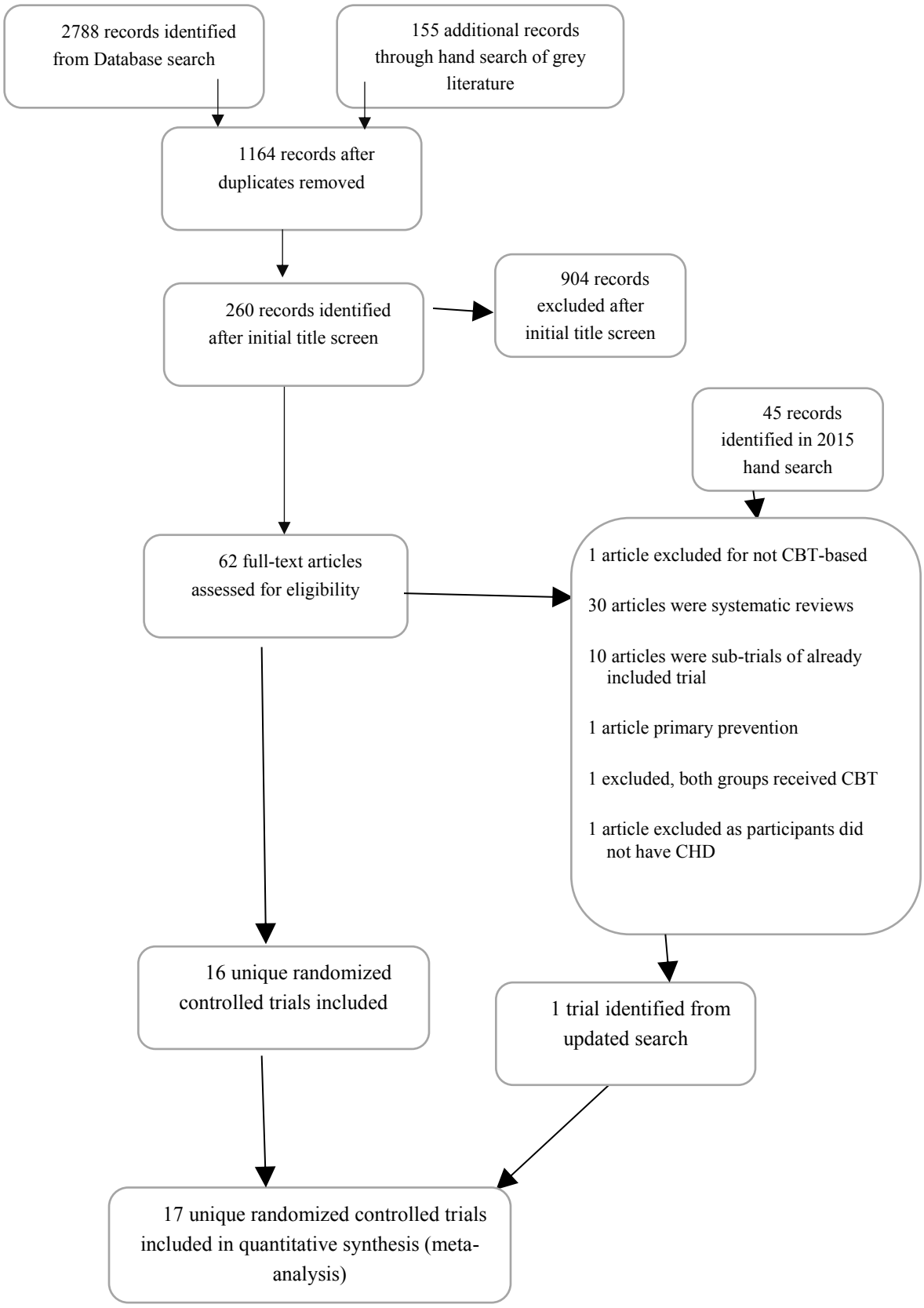
Further inclusion criteria for study eligibility included a year limitation from 1992-current. Management and prevention of CHD as a result of increased knowledge around desired outcomes has changed significantly enough in the past two decades, rendering trials before this date irrelevant. As well, CBT was first suggested and used as a therapy for chronic disease in the late 20$^{th}$ century and for this reason it is not efficient to search earlier than this (Furze et al., 2008). Language was not a formal limit, and if applicable trials published in other languages were identified, a translator was to be accessed and utilized; however, we accepted the possibility that such trials may have to be excluded at that time for feasibility issues.

### 2.3 Search Methods

A systematic search was performed to identify published randomized trials of SP interventions comparing CBT to usual care. The search was developed by this writer in

consultation with the supervisory committee and a health librarian (Refer to Appendix A). The search was first executed in MEDLINE, and then adapted for additional databases, including PsycINFO, EBM Cochrane Controlled Trials, Embase, Scopus, and CINAHL. Sources of grey literature were also included in order to minimize publication bias; clinical trials registries (clinicaltrials.gov), Google Scholar as well as unpublished dissertations and theses were included in the search of grey literature. Meta-analyses that exclude grey literature may increase the risk of exaggerating intervention effects, over-representing studies with statistically significant findings, inflating effect size estimates and may provide less precise effect size estimates (Petticrew & Roberts, 2006). Additionally, published trials tend to be larger and have larger treatment effects than unpublished trials (Higgins & Green, 2011). Conference abstracts were not included due to lack of peer review and detail. Cited reference searches were done via Web of Science or Scopus to look for additional applicable trials. Google scholar was searched manually using keywords "coronary heart disease" and "cognitive behavioural therapy". Hand searching of key journals in this area was performed using the above keywords, including *Journal of Rural Community Psychology, Circulation, British Medical Journal*, *European Journal of Preventive Cardiology, Heart, General Hospital Psychiatry, Psychological Medicine, and Journal of Affective Disorders.* Study selection was done in a 3 tiered process, refer to Table 1 (PRISMA table). In addition, an updated search of clinical trial registries and google scholar was done in early 2015 to identify new applicable trials.

Table 1: PRISMA table for study selection



### 2.4 Study Selection

After the initial search was completed, references were compiled into a reference manager (EndNote), with all reviewers having access. Duplicate references were removed at this time. A preliminary review of the titles and abstracts of citations to identify studies meeting inclusion criteria was initially completed by the writer with the intention of being over inclusive at this stage. Full text was obtained for potentially relevant articles and then reviewed against the previously defined eligibility criteria; a more in-depth and critical review aimed to include only appropriate trials. Two reviewers then independently assessed titles and abstracts for inclusion, the primary author R. Ellis and fellow graduate student L. Mclean. Disagreements were to be resolved by consensus and mediated by a third party, Dr. A Clark as necessary. During title selection, excluded studies were coded by reason for exclusion. In order to ensure methodological quality, this review will satisfy AMSTAR criteria (A Measurement Tool to Assess Systematic Reviews) (Shea et al., 2007). The research question and inclusion criteria were developed a priori, the comprehensive search strategy was documented and used in more than two databases, as well as adapted for the search of grey literature (Shea et al., 2007). A list of both included and excluded studies and their relevant data were maintained and recorded in a standardized data extraction form, in our case Microsoft Excel was utilized (Microsoft, 2013). All initial papers obtained from searching were stored and organized in the reference manager, and backed up weekly by the writer to a cloud service, a USB key and the online version of EndNote (Thompson Reuters, 2014).

### 2.5 Quality Assessment

Although we included only RCTs in attempt to obtain the best evidence to evaluate program effectiveness, even RCTs can vary considerably in quality. Low quality evidence when included

in a systematic review may result in bias, and has the potential to influence the observations of the review; reported outcomes, and effect sizes; ultimately the effectiveness of the intervention being studied may be exaggerated or minimized erroneously (Higgins & Green, 2011). It is therefore important to record the strengths and weaknesses of each included study, regardless of final inclusion. As we were prepared for significant study heterogeneity in terms of quality and components, we decided a priori to not exclude studies based on quality (CRD, 2009). For the purposes of this study, some methodological components were weighted more heavily than others; this will be outlined narratively in the discussion section of this paper (Petticrew & Roberts, 2006). Equally, studies that are not of good quality simply due to poor reporting were not excluded, as the study data were re-analyzed through meta-analysis. In this case, authors were contacted for further information.

The Cochrane Collaboration currently recommends that trial quality be assessed in a narrative-based assessment (Higgins & Green, 2011). The Cochrane quality assessment tool for assessing risk of bias was applied to ameliorate concerns surrounding trial quality (CRD, 2009). In addition Jadad's scale for assessing quality of RCTs was employed during data extraction (Jadad et al., 1996); Cochrane recommends avoiding one single tool in order to sufficiently assess quality (Higgins & Green, 2011). This review therefore assessed selection bias (sequence generation, allocation concealment), performance bias (blinding and other threats to validity), attrition bias (incomplete data and blinding of research staff), detection bias (blinding of outcome assessor) and reporting bias (selective reporting including intention to treat analysis) according to guidelines from the CRD (CRD) (CRD, 2009). The quality assessment tool was used to generate summary assessments of quality and bias for each included study. Two reviewers independently assessed the quality of each included article, and disagreements were resolved by discussion and

consensus. Third party mediation by A. Clark was to be done if necessary. As the reason this meta-analysis is required is due to a lack of high quality evidence, it was anticipated that some of the included trials will include poor descriptions of their interventions. In order to ensure methodological rigour for the final analysis, decisions are made explicit through narrative analysis in Chapter 3 of this manuscript; all attempts were made to ensure our review protocol is explicit and reproducible (Sterne, Gavaghan, & Egger, 2000).

### 2.6 Data Extraction and Management

Data extraction was completed by the primary author using an extraction form developed by the INSPECT team. This form was developed using criteria from the INSPECT taxonomy, developed in 2009 by Clark, Briffa and Redfurn and used in several publications. The INSPECT taxonomy was validated with the involvement of the INSPECT team and with collaboration from 25 'clinician scientist' knowledge users (Clark, 2013a). The final taxonomy has 7 main facets: (1) Target disease population, (2) In-patient program, (3) Program targets, (4) Program ingredients and format, (5) Program delivery, (6) Timing, and (7) Program characteristics (Clark, 2013). Classification of SP interventions was completed through use of a pre-identified taxonomy in order to produce a comprehensive and accurate description of program; this classification was challenging given the heterogeneity and diversity in components of these interventions, including: time of commencement, setting, delivery mechanism, theoretical basis, and provider(s) (Clark, 2013a). The INSPECT data extraction tool was employed for this sub-review to ensure standardized data collection and management throughout all stages of the larger project. Data were managed and stored by the writer using EndNote both on and offline, and subsequently transferred to review manager software endorsed by the Cochrane Collaboration, RevMan 5.3 (The Cochrane Collaboration, 2014). From each included study, demographic and

design information, quality appraisal criteria, program provider, setting, longest length of follow-up and several other program components were extracted according to INSPECT criteria ( Clark, 2013a). Refer to Table 2 for study characteristics. Other applicable information for follow-up with primary authors was included according to criteria set by the Cochrane handbook for systematic reviews (Clark, 2013a). If the required information was not provided in sufficient detail in the manuscripts, the author of the paper was contacted. A total of 13 authors of included trials were contacted for additional information, and all responded. As this review does not access primary data, and no identifying patient information was recorded, the storage and backup of the information did not require ethical review.

Data were collected and organized to ensure that the final included studies were sufficiently homogeneous to measure effect sizes and synthesize data. An estimate of approximately 50-100 papers was expected to meet the initial inclusion criteria from the initial 800 references retrieved. After secondary review and the updated 2015 search, 17 trials met final inclusion criteria, and data subsequently were collected from these. Final papers were also stored in hard copy, with data collection forms attached for efficient retrieval. This was managed by the writer, but remained accessible online to all members of the review team. The writer (and primary reviewer) compared the completed extractions for each study with second reviewer L. Mclean; there were no discrepancies encountered. Sharing and long term archiving will be done via publication and the University of Alberta's Health Research Data Repository (HRDR).

### 2.7 Data Synthesis

Data extracted for the purposes of a systematic review involves a collation, combination and summary of the findings of the included studies. After completion of data extraction, RevMan 5.3 was utilized to complete the statistical analysis for synthesis of evidence (Thompson Reuters,

2014). RevMan is routinely used by knowledge generators to prepare reviews of interventions, methodology, diagnostic test accuracy, and overviews of reviews (The Cochrane Collaboration, 2014); it is the mandatory review tool for developing Cochrane reviews (Higgins & Green, 2011). RevMan is endorsed by the Cochrane Collaboration as a tool for statistical analysis that will "meet the demands of producing high quality systematic reviews of the evidence of the effects of healthcare and deliver these for publication in The Cochrane Library and elsewhere" (Higgins & Green, 2011). Data entry into RevMan was verified by the second reviewer L. Mclean.

Meta-analysis of RCTs has the potential to provide valuable answers to effectiveness questions, as well as the opportunity to settle controversies arising from conflicting claims (CRD, 2009). However, this technique also has potential to seriously mislead knowledge users, particularly if specific study designs, within-study biases, variation across studies, and reporting biases are not carefully and appropriately considered (CRD, 2009). For this reason, the data synthesis plan was made explicit in the protocol, and was completed as follows. Synthesized data is presented both narratively and in table form in Chapter 3 of this manuscript, and includes information concerning outcomes, size and direction of observed effects, and the strength of the evidence. Relationships between and within studies is presented and explored.

Data synthesis begins with the analysis of primary outcomes and calculation of summary statistics for each individual study. In regards to outcome analysis, our review did not identify sufficient data to allow stratified meta-analysis at different common follow-up timings (e.g. 6 or 12, 18 months post randomization), therefore, we pooled studies at their longest follow up. Primary outcomes are as reported previously in this manuscript. Risk ratios (RR) and relative risk ratios (RRR) were calculated for dichotomous outcomes such as cardiac morbidity and all-

cause mortality (Higgins & Green, 2011). Continuous outcomes that did not require standardization (i.e. measured in the same method in each trial) such as blood pressure and total cholesterol levels are measured and reported as mean differences (MD). Other continuous outcomes that were measured using dissimilar scales, including depression, QOL, stress, hostility and anxiety, were reported using standardized mean differences (SMD). All continuous outcomes were measured by calculating the absolute difference between the mean outcomes observed for the intervention and control groups, and reported as effect sizes in a forest plot (J. Higgins & Green, 2011). We intended to report time-to-event outcomes (such as repeat hospitalization or CHD events) by using Kaplan Meier analysis and expressed as a hazard ratios, but time-to-event data were not available from trial manuscripts or through author contact.

Individual studies were then combined for an overall summary of effect size. To evaluate whether CBT interventions were effective when compared to usual care, summary statistics are reported as stated above. Clinical significance was considered by analyzing and reporting absolute effects, and reported thoroughly in the discussion section of this manuscript. Attention to absolute effects is particularly important when considering the clinical application of findings to individual patients who, despite having similar diagnoses, "may have different underlying prognoses and associated risks" (CRD, 2009, p. 64)

Sensitivity analyses was undertaken to determine the strength of the main meta-analysis results. Analyses run with and without the inclusion of certain trials was used to assess the degree to which particular studies (perhaps those with poorer methodology) affected the results. This process may mitigate concerns around publication bias (Petticrew & Roberts, 2006).

Any systematic review of trials addressing one common question will inevitably bring together material with an element of diversity (Higgins & Green, 2011). In statistical terms, the extent to which the results of the trials are consistent is referred to as heterogeneity (CRD, 2009). It was known a priori that this review in particular would be at risk for statistical heterogeneity, as interventions in this area are often poorly described, and report on a wide variety of outcomes (Clark, Redfern, Thompson, & Briffa, 2012). For this reason, a random effects model was used for combining data, as it allows "for between-study variability in results by weighting studies using a combination of their own variance and the between-study variance" (CRD, 2009, p. 55); thus it is more apt a method reflective of the complex nature of SP programs. It remains important to quantify heterogeneity between trials so that appropriate decisions can be made during data interpretation to ensure quality of synthesized data (Higgins & Thompson, 2002). Statistical heterogeneity is reported in Chapter 3 of this manuscript as an $I^2$ statistic, as recommended by Higgins & Thompson (Higgins & Thompson, 2002). The $I^2$ statistic "describes the percentage of total variation across studies that is a due to heterogeneity rather than chance" (Higgins, Thompson, Deeks, & Altman, 2003). Higgins et al. identified, albeit tentatively, that values of 25, 50, and 75% are low, moderate and highly heterogeneous respectively (Higgins et al., 2003). Likewise, Sterne, et al. suggest that substantial heterogeneity due to real differences in the study population, methodology and outcome is indicated by an $I^2$ value >50% and a small p value (<0.10) of the Cochran's *Q* test (Sterne et al., 2000). The CRD guide also offers a rough estimate of heterogeneity using the I2 statistic; 0-40% might not be important, while 30-60% may represent moderate heterogeneity (CRD, 2009). After consideration, for the purposes of this review, an $I^2$ statistic of >40% identifies significant heterogeneity. Results found to be significantly heterogeneous were narratively reported as such, and possible reasons for

inconsistencies investigated and presented in Chapter 4 of this manuscript. As necessary, trials were split into homogenous subgroups and data synthesized within these sub-groups; the $I^2$ statistic was then employed to identify significant subgroups, as well as identify any heterogeneity within them (Higgins et al., 2003). It is important to acknowledge and account for factors contributing to heterogeneity so that reliable conclusions can be drawn from the assembled body of evidence (Borenstein, Hedges, Higgins, & Rothstein, 2009). Pooling of the studies is summarized and presented using forest plots; forest plots provide a clear visual representation of review findings (Borenstein et al., 2009, p. 366). This allows researchers and knowledge users to efficiently determine the precision of individual and pooled results and of the variation between studies (CRD, 2009). Data synthesis was completed with assistance of a healthcare statistician (B. V); the primary author collaborated with B.V. to utilize RevMan 5.3 software, and deliberate upon potential possibilities for data synthesis.

# CHAPTER 3: RESULTS

### 3.1 Study Selection

We initially identified 2788 citations from electronic databases (n = 2788), reference lists (n = 10), trial registries (n= 5) and Google Scholar (n = 166). After the initial screening, we reviewed 256 full manuscripts and excluded 203 of these studies after detailed evaluation (see Figure 1). No disagreements regarding exclusion occurred between the two reviewers. Of the 53 randomized trials that were eligible for inclusion, 12 were either pilot studies, protocol, or were sub-trials of a primary trial already identified for inclusion; we identified 10 trial that reported outcome data from the original 2481 patients from the ENRICHD trial (Enhancing Recovery in Coronary Heart Disease Patients) (Bekke-Hansen, Trockel, Burg, & Taylor, 2012; Berkman et al., 2001; Robert M. Carney et al., 2004; R. M. Carney et al., 2000; Lett et al., 2007; Mendes De Leon et al., 2006; Saab et al., 2009; N. Schneiderman et al., 2004; Trockel, Burg, Jaffe, Barbour, & Taylor, 2008) and two were associated with the Women's Hearts trial; one of these was a pilot study and the other was a background paper (Burell & Granlund, 2002; Claesson et al., 2005). ENRICHD is a large randomized, controlled, multi-center clinical trial sponsored by the National Heart, Lung and Blood Institute in the United States that took place between 1996 and 2001, and included 2481 patients. We referred to the sub-study manuscripts for additional description of the intervention and outcome data as needed. Women's Hearts is a prospective, randomized trial conducted in Sweden between the years 1997 and 2003 that provided a Cognitive Behavioral Therapy (CBT) intervention to 159 women with ischemic heart disease. As with the ENRICHD study, we retrieved data from sub-study manuscripts as necessary.

An updated hand search of Google Scholar and the United States National Library of Medicine clinical trial registry (USNLM) was performed in March 2015, and nine promising trials were identified; three completed trials from Google Scholar and six registered trials from

USNLM. Three trials were excluded immediately for not meeting inclusion criteria, as they were either primary prevention, did not include patients with CHD, or did not employ CBT techniques (Barley et al., 2014; University of Edinburgh, 2000; University of Washington, 2000). We contacted the primary investigators of the remaining six studies for information on availability of data, and all contacted authors responded. None of the five registered clinical trials had results available for the timing of this review; three trials were still in participant recruitment phases (University of Bologna, 2000; Columbia University, 2000; Uppsala University, 2000) and two had manuscripts pending publication and therefore data were unavailable at this time for our purposes (Hospital Italiano de Buenos Aires, 2000; Ying, Lon, Kwang, Wei & Tien, 2013). Of the nine initially promising results, we included one randomized controlled trial (RCT) that was not identified in our original search (Furze et al., 2012). Furze et al. compared a CBT-based angina program to care from a specialized nurse for adult outpatients with angina, thus met our inclusion criteria (Furze et al., 2012).

Data were synthesized for outcomes reported by two or more trials according to recommendations of the Cochrane Collaboration (Higgins & Green, 2011). Of note, two trials that met inclusion criteria and were included in this review did not contribute to the data synthesis because the reported outcomes were incongruent with the other included studies; for example, Gidron (1999) was the only trial that measured and reported Hostility, and Tisminetzky (2011) was the only trial to measure and report latent class and transition analyses on depression (Gidron, Davidson, & Bata, 1999a; Tisminetzky, Bray, Miozzo, Aupont, & McLaughlin, 2011). In both cases, no supplementary outcome data were available through communication with authors.

Data were synthesized for the following outcomes: depression, anxiety, stress, quality of life, all-cause mortality, cardiovascular morbidity (including repeat cardiovascular events, hospitalization for cardiovascular causes, unplanned revascularization), and changes in total cholesterol and systolic blood pressure. We intended to extract data separately for the individual determinants of cardiovascular morbidity, including hospitalization and repeat myocardial infarction, but were unable to as a result of the high heterogeneity of the reported outcomes. We were not able to extract or synthesize data on the remainder of our outcomes of interest, including body mass index (BMI), smoking, hostility, and cost effectiveness due to a lack of reporting and general lack of follow up data beyond one year; only two trials reported cost-effectiveness data, and incongruence of trial outcome reporting on BMI, smoking rates and hostility prevented us from evaluating these.

Consequently, 17 randomized controlled trials that evaluated the effectiveness of CBT for secondary prevention (SP) of coronary heart disease (CHD) were included in the review. Identified trials were diverse in terms of control groups used; trials compared CBT to control groups who received either traditional cardiac rehabilitation (CR), usual care, or specialist care. Reported outcomes were variable, refer to Table 2 for characteristics of included studies.

Table 2: Characteristics of Studies

| STUDY ID (Author, Year) | SAMPLE SIZE (n) | LONGEST FOLLOW UP (months) | MEAN AGE (yrs) | MALE GENDER (%) | KEY COMPONENTS OF INTERVENTION | CONTROL COMPARISON | REPORTED OUTCOMES | MODALITY |
|---|---|---|---|---|---|---|---|---|
| *Blom 2009* | 57 | 17 | 62 | 0 | 20x 2 hr sessions, Nurse provider, outpatient clinic | Usual medical care | Stress, social support | Multi |
| *Claesson 2005* | 159 | 24 | 60.5 | 0 | 20x2hr sessions over 1 yr, single provider (unknown discipline), outpatient setting, tailored to women | Specialist care | Depression, CV morbidity, Stress, cholesterol | Single |
| *Dalal 2007* | 104 | 9 | 61-64 | 80.7 | Nurse provider, little provider contact, Heart Manual, home setting | Traditional CR | Depression, Anxiety, QOL, Cholesterol, smoking | Multi |
| *Doering 2007* | 52 | 6 | 58-63 | 0 | 8x1 hour sessions, nurse provider, home setting | Specialist care | Depression, NK cell function, post-op illness | Single |
| *Berkman (ENRICHD) 2003* | 2481 | 6 | 61 | 56 | Weekly sessions, group format, psychologist provider, outpatient setting | Specialist care | All-cause mortality, Depression, QOL, CV morbidity, | Single |
| *Fernandez 2009* | 51 | 2.5 | 57 | 78 | 3xphone calls, 8 weeks, provider GP and research assistant, home setting | Specialist care | Cv morbidity, Cholesterol, BP, fruit/veg intake, BMI | Multi |
| *Freedland 2009* | 43 | 9 | 61.5 | 50.6 | Weekly 1 hr sessions, SW or psychologist provider, outpatient setting | Usual medical care | Stress, Anxiety, Depression, cognition, hopelessness | Single |
| *Gidron 1999* | 22 | 2 | No Data | 100 | 8x90min weekly group meetings (for hostility), at-home log | Specialist care | BP, Hostility | Single |
| *Lewin 2002* | 130 | 6 | 67 | 60 | Angina Plan self-help manual, nurse provider, 10min phone calls every 2 weeks | Specialist care | Depression, CV morbidity, Anxiety, BP, QOL | Multi |

| STUDY ID (Author, Year) | SAMPLE SIZE (n) | LONGEST FOLLOW UP (montl | MEAN AGE (yrs | MALE GENDER (%) | KEY COMPONENTS OF INTERVENTION | CONTROL COMPARISON | REPORTED OUTCOMES | MODALITY |
|---|---|---|---|---|---|---|---|---|
| *Gullickson 2011* | 362 | 94 | 61.5 | 76.5 | 20x2 hr sessions, nurse or psychologist provider, outpatient clinic, self monitoring | Specialist care | Cv morbidity, All-cause mortality | Multi |
| *Jolly 2007* | 525 | 12 | 61.5-62.5 | 76.6 | Nurse provider, 3 home visits, 1 phone call, Heart Manual, home setting | Traditional CR | Depression, Anxiety, BP, Cholesterol. | Multi |
| *Koertge 2008* | 247 | 18 | 62 | 0 | 20x2 hr sessions, group based, outpatient, | Specialist care | Depression, Stress (Vital exhaustion), All-cause mortality | Multi |
| *Murphy 2013* | 275 | 12 | 58-59.9 | 86.5 | 8 weeks, group based, outpatient, psychologist provider, homework | Usual medical care | Depression, Anxiety, QOL, Social Support, Cholesterol | Multi |
| *Orth-Gomer 2009* | 237 | 85.2 | 61.5 | 0 | CBT-trained nurse providers, | Usual medical care | All-cause mortality | Multi |
| *Tsminetsky 2011* | 100 | 6 | 60 | 67 | Depressed/anxious pts, 8xwkly 30min individual sessions, Psychologist or Psychiatrist provider | Specialist care | Depression/Anxiety via Latent Class Analysis | Multi |
| *Turner 2012* | 57 | 12 | 61.5 | 74 | 1.5hrs x6 wk group sessions, providers psychologists, standardized manual w homework | Traditional CR | Depression, Anxiety | Multi |
| *Furze 2012* | 158 | 6 | 64-65 | 52.3 | The Angina plan, lay-person facilitator, brief phone calls, home or individual based | Specialist care | All-cause mortality, CV morbidity, BP, Cholesterol. | Multi |

### 3.2 Quality Assessment

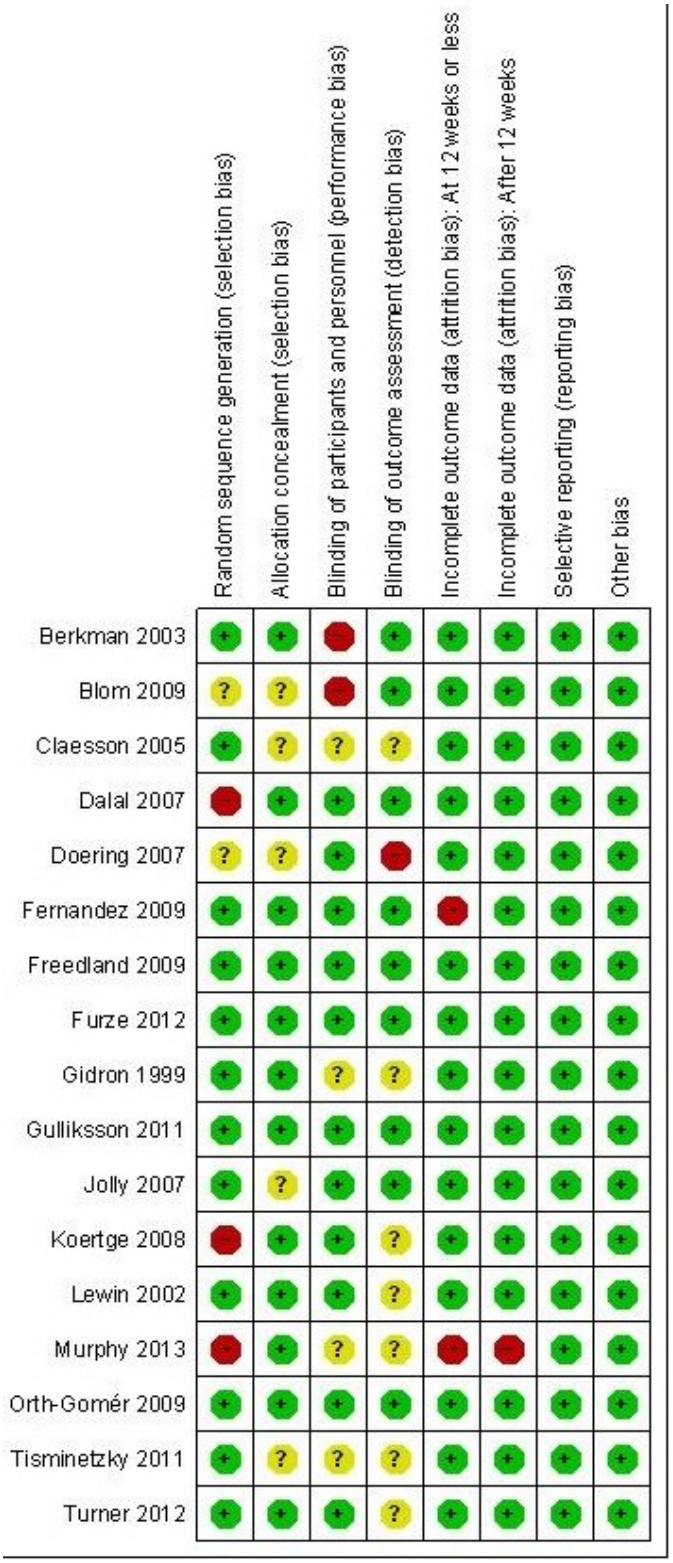
The quality of the included trials was variable but of overall moderate quality (refer to Table 3 for risk of bias table). Primarily, we found a deficiency in the reporting of germane methodological details. This lack of clarity in the reporting of trials made quality assessment difficult; specifically, a number of studies did not report sufficient methodological detail, particularly with respect to random sequence generation, allocation concealment, and participant or outcome assessor blinding, in order to allow full assessment of potential risk of bias. As our included trials were randomized and controlled, information on randomization procedures should be clearly reported (Higgins & Green, 2008). Although these methods were underreported, studies did provide sufficient data on baseline characteristics of participants. Control and intervention participants were sufficiently similar in these trials to assuage our concerns around lack of random sequence generation and allocation concealment. Detail was also generally lacking on blinding of participants and outcome assessors. First, it is almost impossible to blind participants who are receiving a complex intervention or not; for example, in the ENRICHD trial, patients either had no further follow-up aside from their cardiologist (classified as SC), or a group-based intervention (Berkman et al., 2003). Lack of participant blinding would more likely affect outcomes measured by patient reporting, such as depression; only three of the 11 trials measuring depression were of poor or uncertain quality in terms of blinding (Claesson, 2005; Berkman, 2003; Murphy, 2013). Poor detail on blinding of outcome assessors was also unlikely to have affected our conclusions; the majority of outcomes were measured using patient reported scales. Morbidity and mortality data are also unlikely to be significantly affected by blinding of outcome assessors (Petticrew & Roberts, 2006).

From methods that were reported, the most common weaknesses were: small sample sizes, short follow-up period, and lack of blinding of participants or outcome assessors. Blinding concerns were addressed above. Sample sizes can be variable, particularly in social sciences research (Petticrew & Roberts, 2006). While smaller sample sizes may have concerns around power of results, in our case sample sizes were less likely to influence outcomes, as the pooling of smaller studies in meta-analysis ameliorates some of these concerns (Higgins & Green, 2011). Short follow up periods is a common constraint in clinical trials, and can lead to effects of censoring (Prinja, Gupta & Verma, 2010). Censoring refers to a lack of information on a time to event outcome due to either loss to follow up or a non-occurrence of outcome event before the trial end (Prinja, Gupta, & Verma, 2010). This is an unfortunate situation that should be better addressed; the value of longer follow up periods in the evaluation of programs aimed at secondary prevention of chronic illnesses such as CHD should be clear. Long-term benefits such as reductions in symptoms, even mortality, resultant from improvements in psychosocial outcomes such as depression, QOL, anxiety and stress will likely not be actualized in such short follow-up periods (Stone, Clark, & Arena, 2009). The insidiousness and chronicity of coronary disease requires longer follow up to see real reductions in mortality and morbidity (Stone et al., 2009).

Poor quality should be differentiated from bias. Poor methodological quality does not inevitably equal a deviation from the truth in terms of outcomes; further, it should not be assumed that poor quality led to an overestimation of effect. The deficiencies both in terms of reporting and methodological quality can be considered relatively inconsequential in terms of exerting an effect on conclusions of this review.

Table 3: Risk of Bias Summary

*Risk of Bias Table*



### 3.3 Data Extraction and Management

Data extraction followed the review protocol, as previously described (refer to Chapter 2). We encountered one logistical problem in the extraction of the data; the data extraction tool developed for INSPECT was not compatible with the review manager software, RevMan 5.3, and therefore data had to be manually extracted into both the tool and the software. This led to significant time delays. Data management was congruent with the review protocol, and managed using EndNote, Microsoft Excel, and RevMan.

### 3.4 Data Synthesis

#### 3.4.1 Continuous Outcomes

Eleven of the seventeen included trials reported depression outcomes (Berkman et al., 2003; Claesson et al., 2005; Dalal, Evans, et al., 2007; Doering, Cross, Vredevoe, Martinez-Maza, & Cowan, 2007; Freedland et al., 2009; Furze et al., 2012; Jolly, Lip, et al., 2007; Koertge, Janszky, Sundin, Blom, Georgiades, Lajszla, et al., 2008; Lewin et al., 2002; Murphy et al., 2013; Turner, Hambridge, Baker, Bowman, & McElduff, 2012). These trials measured depression using the Beck Depression Inventory (BDI), the BDI II, or the Hospital Anxiety and Depression Scale (HADS). These are well validated scales with clinically similar components and instruments, thus we were able to directly compare the results (Higgins & Green, 2008). CBT-interventions were more desirable in terms of depression– being more effective at reducing depression when compared to non-CBT based cardiac rehabilitation (CR), usual care or specialist care (11 trials, n=3133, 95% CI -0.29: -0.50 to -0.08). CBT-based interventions were more beneficial when compared to specialist care, either when provided as a single modality (2 trials, n=96, 95% CI: 0.70: -1.11 to -.028) (Doering, et al., 2007; Freedland et al., 2009) or multi-modality intervention (2 trials, n=272, 95% CI -0.30: -0.54 to -0.06) (Furze et al., 2012; Lewin et

al., 2002). Multi-modality CR interventions with a CBT basis were as effective as comprehensive CR without such a basis (4 trials, n=781, 95% CI -0.17: -0.77 to 0.43) (Claesson et al., 2005; Dalal et al., 2007; Jolly et al., 2007; Turner et al., 2012) and showed similar or positive effects over usual care in all trials (3 trials, 95% CI 0.25: -0.52 to 0.02) (Berkman et al., 2003; Koertge et al., 2008; Murphy et al., 2013).

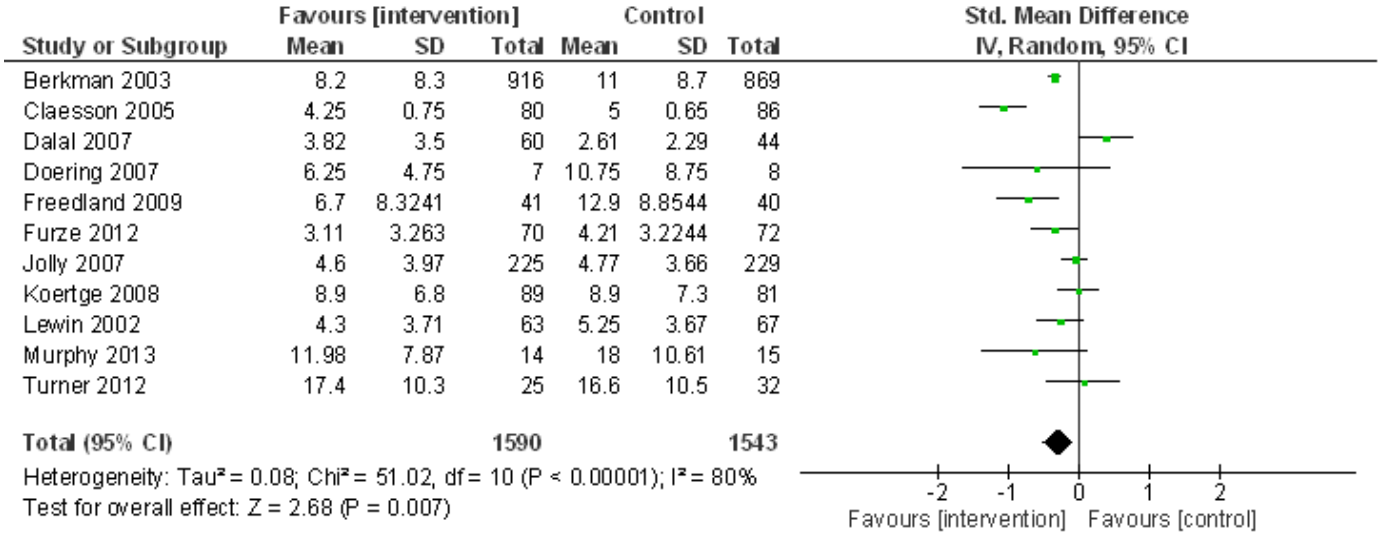



Table 3.1: Depression

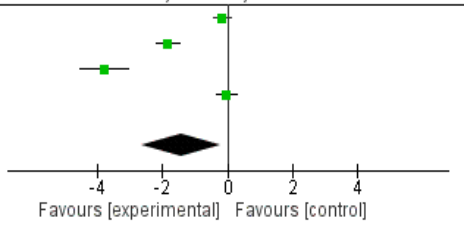
Four trials provided data for changes in stress outcomes (Blom et al., 2009; Claesson et al., 2005; Freedland et al., 2009; Koertge et al., 2008). Stress was measured using the Perceived Stress Scale and the Everyday Life Stress Scale, which were clinically comparable. We also included within this analysis measurement of vital exhaustion, as this is utilized as a marker of psychological stress (Raikkonen, 1997). Vital exhaustion was measured in one trial, using the Maastricht Questionnaire (Koertge et al., 2008). CBT-based interventions were more beneficial than non-CBT based interventions in terms of stress reduction (4 trials, n=642, 95%CI -1.41: -

2.64 to -0.19) (Blom et al., 2009; Claesson et al., 2005; Freedland et al., 2009; Koertge et al., 2008).

Table 3.2 Stress

| | Intervention | | | Control | | | | Std. Mean Difference |
|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI |
| Blom 2009 (1) | 34 | 7.8 | 113 | 35.3 | 8.7 | 122 | 25.6% | -0.16 [-0.41, 0.10] |
| Claesson 2005 (2) | 13.25 | 1.5 | 80 | 16.25 | 1.75 | 86 | 25.3% | -1.83 [-2.19, -1.46] |
| Freedland 2009 (3) | 14 | 1.2 | 41 | 18.6 | 1.2 | 40 | 23.6% | -3.80 [-4.54, -3.06] |
| Koertge 2008 | 16.5 | 11.1 | 88 | 16.9 | 11.3 | 72 | 25.5% | -0.04 [-0.35, 0.28] |
| **Total (95% CI)** | | | **322** | | | **320** | **100.0%** | **-1.41 [-2.63, -0.19]** |

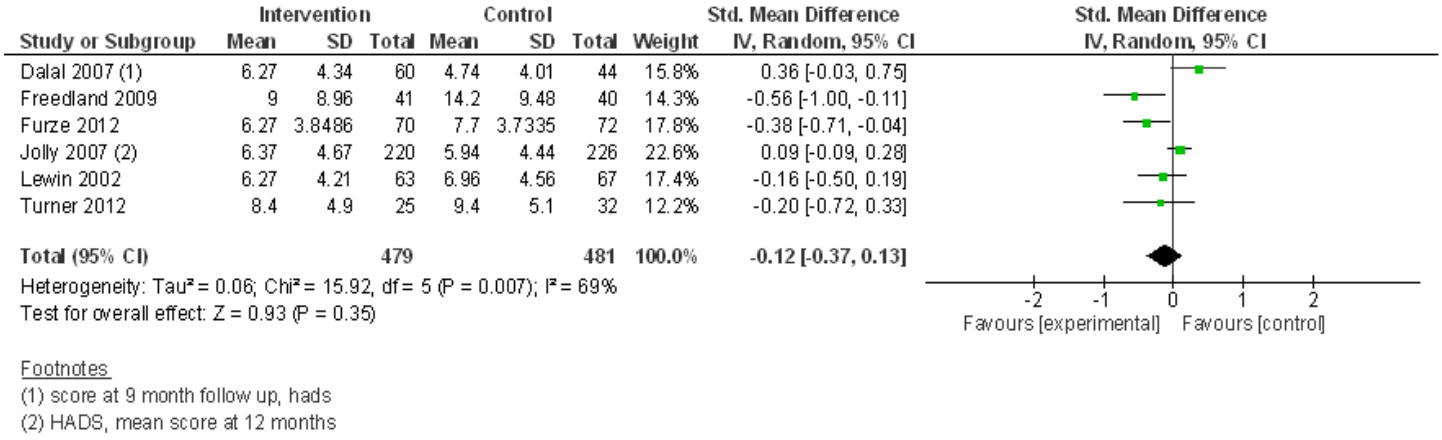
Heterogeneity: Tau² = 1.50; Chi² = 138.66, df = 3 (P < 0.00001); I² = 98%
Test for overall effect: Z = 2.26 (P = 0.02)




Footnotes
(1) Daily stress behaviour - assessed with Everyday Life Stress Scale (ELSS), used scores from longest period of measurement (1-2yr follow up)
(2) self-rated stress behaviour (SSSB), assessed via Everyday Life Stress Scale (ELSS)
(3) perceived stress scale, p. 392

Six of the seventeen trials included anxiety outcomes (Dalal, Evans, et al., 2007a; Freedland et al., 2009a; Furze et al., 2012; Jolly, Lip, et al., 2007; R. J. P. Lewin et al., 2002a; Turner et al., 2012). The HADS anxiety sub-scale and Beck Anxiety Inventory (BAI) are clinically comparable scales (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961; Hamilton, 1960; Zigmond & Snaith, 1983). Similar to depression, multi-modality CBT-based interventions were more beneficial than specialist care alone (2 trials, n=272, 95% CI 0.27(-0.51 to -0.03) (Furze et al., 2012; R. J. P. Lewin et al., 2002b), however, CBT based multi-modality interventions showed no added benefits over cardiac rehabilitation alone (3 trials, n=607,95% CI: 0.12 -0.12 to 0.35) (Dalal, Evans, Campbell, Taylor, Watt, Read, Mourant, Wingham, Thompson, & Pereira Gray, 2007; Jolly et al., 2007; Turner et al., 2012).

Table 3.3 Anxiety



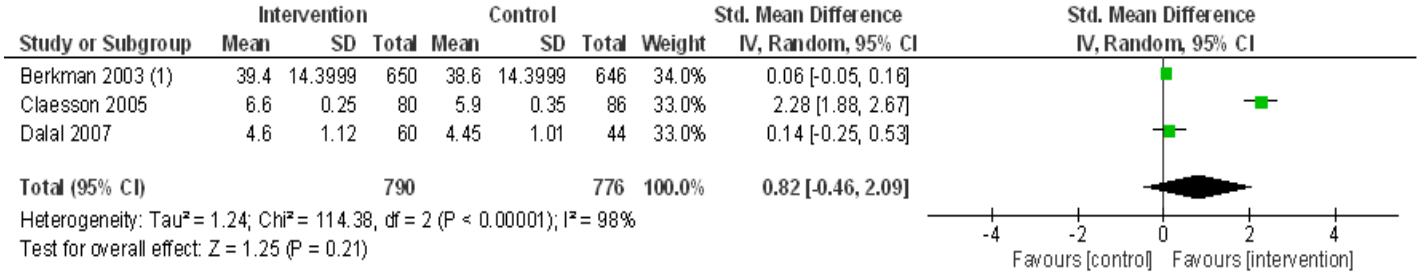
| Study or Subgroup | Intervention Mean | SD | Total | Control Mean | SD | Total | Weight | Std. Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Dalal 2007 (1) | 6.27 | 4.34 | 60 | 4.74 | 4.01 | 44 | 15.8% | 0.36 [-0.03, 0.75] |
| Freedland 2009 | 9 | 8.96 | 41 | 14.2 | 9.48 | 40 | 14.3% | -0.56 [-1.00, -0.11] |
| Furze 2012 | 6.27 | 3.8486 | 70 | 7.7 | 3.7335 | 72 | 17.8% | -0.38 [-0.71, -0.04] |
| Jolly 2007 (2) | 6.37 | 4.67 | 220 | 5.94 | 4.44 | 226 | 22.6% | 0.09 [-0.09, 0.28] |
| Lewin 2002 | 6.27 | 4.21 | 63 | 6.96 | 4.56 | 67 | 17.4% | -0.16 [-0.50, 0.19] |
| Turner 2012 | 8.4 | 4.9 | 25 | 9.4 | 5.1 | 32 | 12.2% | -0.20 [-0.72, 0.33] |
| **Total (95% CI)** | | | **479** | | | **481** | **100.0%** | **-0.12 [-0.37, 0.13]** |

Heterogeneity: Tau² = 0.06; Chi² = 15.92, df = 5 (P = 0.007); I² = 69%
Test for overall effect: Z = 0.93 (P = 0.35)



Footnotes
(1) score at 9 month follow up, hads
(2) HADS, mean score at 12 months

Three trials reported changes in quality of life (QOL) (Berkman et al., 2003; Claesson et al., 2005; Dalal et al., 2007). QOL was measured using a variety of combined questionnaires which were all clinically comparable; nonetheless, differences between means were standardized as with other psychosocial outcomes. CBT-based interventions were as effective as usual care, specialist care or traditional CR (95% CI 0.82: -0.46 to 2.09; p=0.21).



| Study or Subgroup | Intervention Mean | SD | Total | Control Mean | SD | Total | Weight | Std. Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Berkman 2003 (1) | 39.4 | 14.3999 | 650 | 38.6 | 14.3999 | 646 | 34.0% | 0.06 [-0.05, 0.16] |
| Claesson 2005 | 6.6 | 0.25 | 80 | 5.9 | 0.35 | 86 | 33.0% | 2.28 [1.88, 2.67] |
| Dalal 2007 | 4.6 | 1.12 | 60 | 4.45 | 1.01 | 44 | 33.0% | 0.14 [-0.25, 0.53] |
| **Total (95% CI)** | | | **790** | | | **776** | **100.0%** | **0.82 [-0.46, 2.09]** |

Heterogeneity: Tau² = 1.24; Chi² = 114.38, df = 2 (P < 0.00001); I² = 98%
Test for overall effect: Z = 1.25 (P = 0.21)



Footnotes
(1) Data from Mendes de Leon (2006), the same population as ENRICHD, only used SF-12 PCS. Had to calculate SD from MD

Table 3.4: Quality of Life

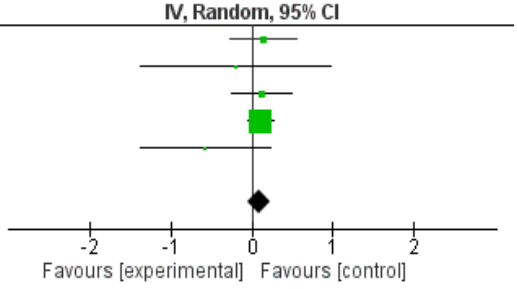
### 3.4.2 Modifiable Risk Factor Outcomes

Five trials measured and reported changes in blood pressure (Claesson et al., 2005; Fernandez et al., 2009; Furze et al., 2012; Gidron, Davidson, & Bata, 1999; Jolly et al., 2007), and five trials reported changes in total cholesterol (Dalal, Zawada, Jolly, Moxham, & Taylor, 2010; Fernandez et al., 2009; Furze et al., 2012; Jolly et al., 2007; Murphy et al., 2013); three reported both. We considered changes in systolic blood pressure (SBP) only, as SBP is the number used by the Framingham Heart Study group to calculate future cardiovascular risk (D'Agostino et al., 2008). Meta-analysis exposed a non-significant improvement in systolic blood pressure for the CBT intervention group (p=0.82). The SMD for trials reporting SBP was -0.02 (95% CI -0.16 to 0.13, p for heterogeneity=0.42, $I^2$ 0%). We also found a non-significant overall improvement in total cholesterol levels for the control groups (p=0.18). The SMD for trials reporting total cholesterol was 0.09 (95% CI, -0.04 to 0.23, p for heterogeneity=0.55, $I^2$ 0%).

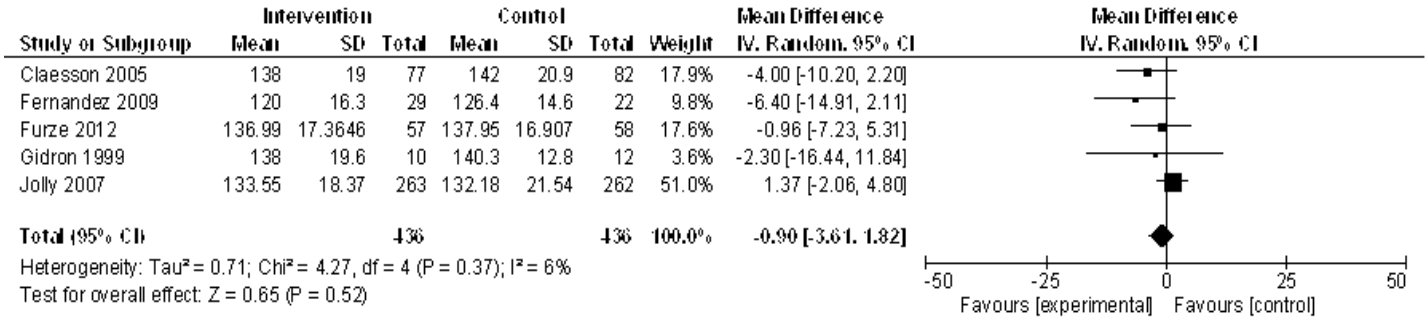
Table 3.4: Total Cholesterol

| | Intervention | | | Control | | | | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI |
| Dalal 2007 (1) | 4.6 | 1.12 | 60 | 4.45 | 1.01 | 44 | 10.6% | 0.15 [-0.26, 0.56] |
| Fernandez 2009 (2) | 4.1 | 1.3 | 29 | 4.3 | 2.6 | 22 | 1.3% | -0.20 [-1.39, 0.99] |
| Furze 2012 | 4.27 | 1.1713 | 70 | 4.15 | 1.1031 | 72 | 12.8% | 0.12 [-0.25, 0.49] |
| Jolly 2007 (3) | 3.99 | 0.9 | 232 | 3.88 | 0.83 | 233 | 72.5% | 0.11 [-0.05, 0.27] |
| Murphy 2013 (4) | 3.71 | 0.86 | 14 | 4.29 | 1.32 | 15 | 2.8% | -0.58 [-1.39, 0.23] |
| **Total (95% CI)** | | | **405** | | | **386** | **100.0%** | **0.09 [-0.04, 0.23]** |

Heterogeneity: Tau² = 0.00; Chi² = 3.05, df = 4 (P = 0.55); I² = 0%
Test for overall effect: Z = 1.35 (P = 0.18)




Footnotes
(1) mean change and CI data available
(2) mean at baseline
(3) SMD and MD available.
(4) From Turner paper



| Study or Subgroup | Intervention Mean | SD | Total | Control Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Claesson 2005 | 138 | 19 | 77 | 142 | 20.9 | 82 | 17.9% | -4.00 [-10.20, 2.20] |
| Fernandez 2009 | 120 | 16.3 | 29 | 126.4 | 14.6 | 22 | 9.8% | -6.40 [-14.91, 2.11] |
| Furze 2012 | 136.99 | 17.3646 | 57 | 137.95 | 16.907 | 58 | 17.6% | -0.96 [-7.23, 5.31] |
| Gidron 1999 | 138 | 19.6 | 10 | 140.3 | 12.8 | 12 | 3.6% | -2.30 [-16.44, 11.84] |
| Jolly 2007 | 133.55 | 18.37 | 263 | 132.18 | 21.54 | 262 | 51.0% | 1.37 [-2.06, 4.80] |
| **Total (95% CI)** | | | 436 | | | 436 | 100.0% | **-0.90 [-3.61, 1.82]** |

Heterogeneity: Tau² = 0.71; Chi² = 4.27, df = 4 (P = 0.37); I² = 6%
Test for overall effect: Z = 0.65 (P = 0.52)

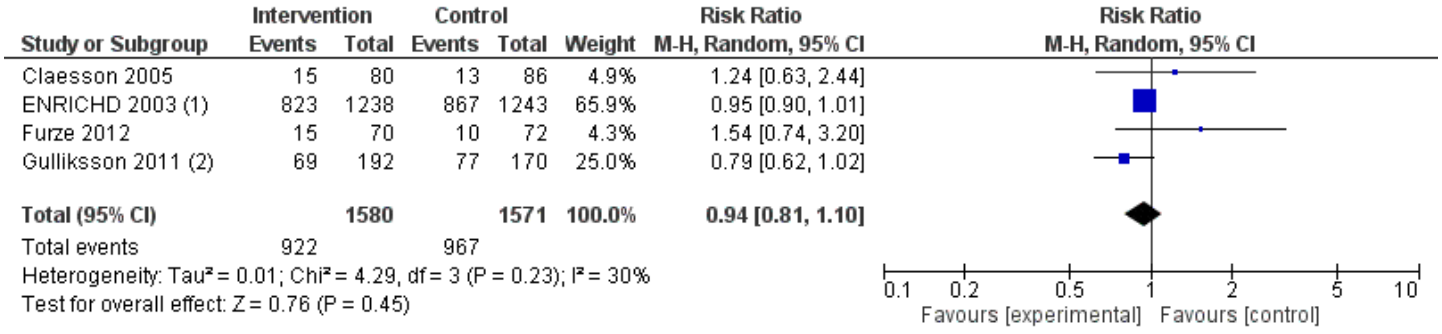


Table 3.5: Systolic Blood Pressure

### 3.4.3 Dichotomous Outcomes

Four trials reported data on cardiovascular morbidity (Berkman et al., 2003; Claesson et al., 2005); ten trials provided all-cause mortality data (Berkman et al., 2003; Claesson et al., 2005; Dalal et al., 2007; Furze et al., 2012; Gulliksson et al., 2011; Jolly et al., 2007; Koertge et al., 2008; Lewin et al., 2002; Orth-Gomér et al., 2009; Turner et al., 2012); three reported both. While we did not find a significant difference between treatment effects, and individual trial results were somewhat heterogeneous (p=0.45 and p=0.19; $I^2$ 30% and 51% respectively), we founds trends favouring CBT-based interventions. Multiple modality interventions underpinned by CBT had favorable non-significant effects on morbidity (3 trials, n=572, 95% CI 0.85: 0.67 to 1.08) as well as all-cause mortality (3 trials, n= 2965, 95% CI: 0.52: 0.22 to 1.23)

Table 3.5: Cardiovascular Morbidity



| Study or Subgroup | Intervention Events | Total | Control Events | Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Claesson 2005 | 15 | 80 | 13 | 86 | 4.9% | 1.24 [0.63, 2.44] |
| ENRICHD 2003 (1) | 823 | 1238 | 867 | 1243 | 65.9% | 0.95 [0.90, 1.01] |
| Furze 2012 | 15 | 70 | 10 | 72 | 4.3% | 1.54 [0.74, 3.20] |
| Gulliksson 2011 (2) | 69 | 192 | 77 | 170 | 25.0% | 0.79 [0.62, 1.02] |
| **Total (95% CI)** | | **1580** | | **1571** | **100.0%** | **0.94 [0.81, 1.10]** |
| Total events | 922 | | 967 | | | |

Heterogeneity: Tau² = 0.01; Chi² = 4.29, df = 3 (P = 0.23); I² = 30%
Test for overall effect: Z = 0.76 (P = 0.45)

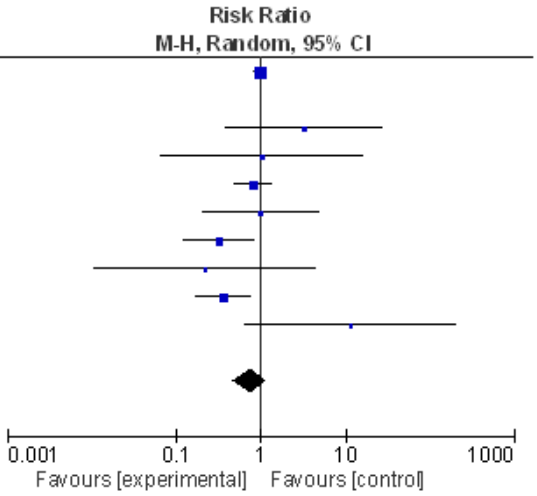


Footnotes
(1) recurrent MI (nonfatal), revascularization, CV hospitalization
(2) non fatal CVD ONLY (not AMI, see note on paper)

Table 3.6: All-cause Mortality

| Study or Subgroup | Intervention Events | Total | Control Events | Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Berkman 2003 | 168 | 1238 | 172 | 1243 | 29.9% | 0.98 [0.80, 1.19] |
| Claesson 2005 | 0 | 77 | 0 | 80 | | Not estimable |
| Dalal 2007 | 4 | 40 | 1 | 32 | 4.0% | 3.20 [0.38, 27.24] |
| Furze 2012 | 1 | 70 | 1 | 72 | 2.5% | 1.03 [0.07, 16.13] |
| Gulliksson 2011 | 23 | 192 | 25 | 170 | 22.3% | 0.81 [0.48, 1.38] |
| Jolly 2007 | 3 | 263 | 3 | 262 | 6.6% | 1.00 [0.20, 4.89] |
| Koertge 2008 | 5 | 119 | 17 | 128 | 13.2% | 0.32 [0.12, 0.83] |
| Lewin 2002 | 0 | 68 | 2 | 74 | 2.1% | 0.22 [0.01, 4.45] |
| Orth-Gomér 2009 | 8 | 112 | 25 | 125 | 17.0% | 0.36 [0.17, 0.76] |
| Turner 2012 | 4 | 25 | 0 | 32 | 2.3% | 11.42 [0.64, 202.72] |
| **Total (95% CI)** | | **2204** | | **2218** | **100.0%** | **0.74 [0.47, 1.16]** |
| Total events | 216 | | 246 | | | |

Heterogeneity: Tau² = 0.17; Chi² = 16.35, df = 8 (P = 0.04); I² = 51%
Test for overall effect: Z = 1.31 (P = 0.19)




### 3.4.4 Publication Bias

Egger tests were performed for the most significant outcomes that included enough trials, depression and all-cause mortality. The p-value of the Egger test for depression was 0.08, and for all-cause mortality was 0.74. As both these p-values are non-significant, publication bias is likely minimal and thus has not affected review quality.

Table 3.8 Funnel Plot for Depression

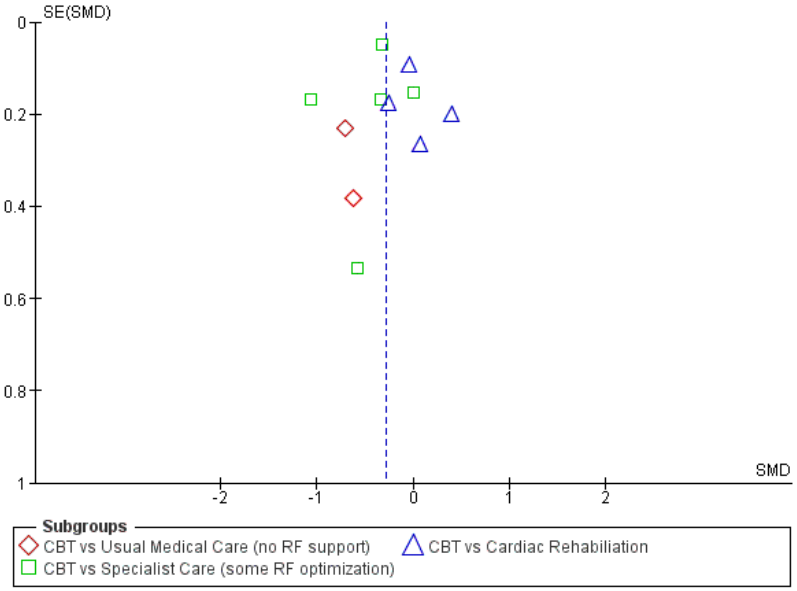
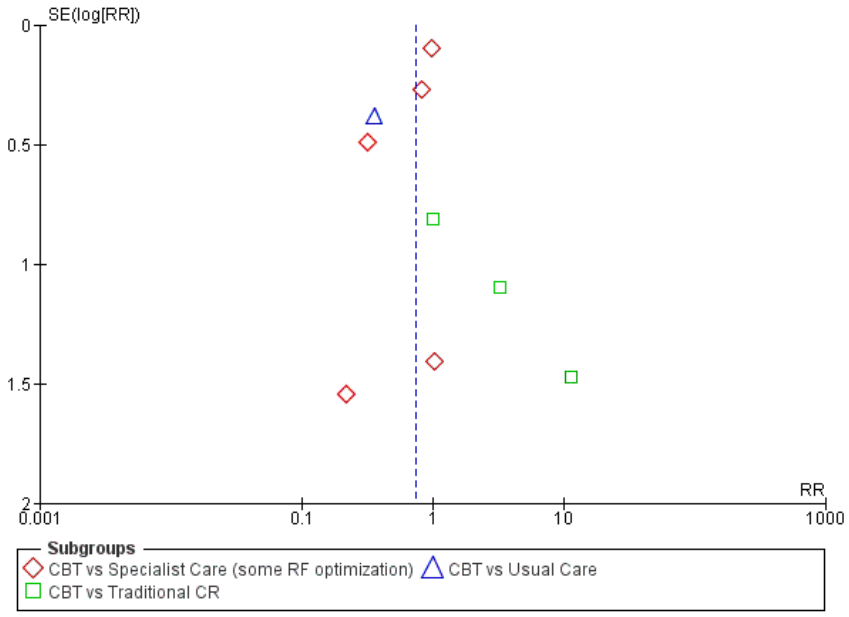


Table 3.9: Funnel Plot for All-cause mortality



# CHAPTER 4: DISCUSSION AND RECOMMENDATIONS

## 4.1 Discussion

### 4.1.1 Effectiveness of CBT

Depression is more successfully improved through secondary prevention programs based on CBT than other non CBT-based interventions for CHD. In fact, the benefits of CBT-based interventions were seen even when it was provided in isolation from a formal cardiac rehabilitation (CR) program. The positive results we found concerning the effectiveness of CBT-based interventions leads the way for an adjustment in how we approach secondary prevention of CHD. CBT-based interventions were more effective at reducing depression, when compared to all controls including non-CBT based CR, usual care or specialist care. Further, CBT-based interventions retained their benefits when compared to usual care or specialist care, either when provided as a single or multi-modality intervention.

When provided as part of a multi-modality SP program, CBT-based interventions are at least as safe and efficacious when compared to comprehensive CR in terms of depression, anxiety, stress, quality of life, systolic BP, total cholesterol, all-cause mortality, and morbidity.

Indeed, cardiovascular (CV) morbidity and all-cause mortality trends favouring CBT-based interventions give support for the use of CBT as part of SP programs for CHD. Unfortunately, only nine trials provided data on all-cause mortality; authors of all other trials were contacted to ascertain morbidity and mortality data, none of whom were able to provide these data. Data were unavailable primarily due to lack of funding for further follow-up. In this review, CV morbidity referred to repeat myocardial infarction (MI), hospitalization for cardiac causes, and repeat revascularization. Trends favoured the CBT intervention groups, although this finding was not

statistically significant. Interestingly, the favourable findings for the CBT intervention groups were relatively consistent between studies.

All-cause mortality and CV morbidity trends in our review were congruent with previous data on morbidity and mortality; Clark et al. found no significant difference between the CBT-based Heart Manual and standard CR in terms of GP visits, cardiac symptoms, cardiac events and death rate (Clark, Kelly, & Deighan, 2011). In our review, Orth-Gomer et al found a risk ratio of 0.36 (95% CI 0.17 to 0.76) while Koertge et al. found a risk ratio of 0.32 (95% CI 0.12 to 0.83) for a total sample size of 231 patients (Koertge et al., 2008; Orth-Gomer et al., 2009). Conversely, Turner (2012) and Dalal (2007) reported mortality rates slightly favouring controls (Dalal et al., 2007; Turner, Hambridge, Baker, Bowman, & McElduff, 2012). Both of these trials had relatively small sample sizes, which limited their power and contribution to pooled effects (n=57 and 72 respectively). Secondary analysis that excluded these two trials influenced the results enough to almost make pooled effects statistically significant (from p=0.19 to p=0.06).

CBT interventions, based on this review, are as or more effective as other alternatives - usual care, specialist care, and traditional CR programs. The potential reduction in morbidity and mortality risk that CBT interventions offer is also motivating and should be investigated further with additional secondary analysis once enough data are available that consistently report intervention components and outcomes.

If CBT interventions do indeed offer additional reduction in mortality and or mortality risk for patients with CHD, and if additional data demonstrate cost-effective delivery of CBT interventions, the application of CBT-based interventions to secondary prevention program guidelines may be warranted. As CBT-based interventions require a single provider, it can be

implemented in any setting, in a group or individual format, and is relatively flexible compared to comprehensive CR, potential advantages in terms of cost and feasibility may well be appealing to providers, health systems and patients.

Although cost-effectiveness data are increasingly available for studies that evaluate secondary prevention programs for CHD, they remain insufficient to accurately examine costs versus benefit of these SP interventions. The lack of these data was particularly evident in our review; we were able to identify only two of our seventeen included trials that had cost-effectiveness data available (Jolly et al., 2007; Taylor et al., 2007).

### 4.1.2 Poor Quality of Trials

We have known for a long time that published research on complex healthcare interventions does not sufficiently describe components of tested interventions, excessively simplifies and decontextualizes them, and/or does not seek to understand why they work (Clark, Redfern, et al., 2012). Part of this lack of information is resultant from poor reporting; recent research found that only 39% of 137 of such interventions were adequately reported (Hoffmann, Erueti, & Glasziou, 2013). This knowledge of deficiencies in the reporting and quality of non-pharmacological trial does not yet appear to be influencing published research in this area; as we anticipated, poor reporting was indeed problematic in our review.

A significant weakness in the quality of our included trials was relatively short follow-up periods that were insufficient to gather data around long-term effectiveness of CBT-based interventions. The most common follow-up period (mode) was six months, although the mean was 19.2 months, the standard deviation of 27.1 months, indicating significant diversity (refer to Table 1). The significance of short follow-up periods is such that the true effects on morbidity

and mortality may not yet be seen given the natural history of atherosclerotic CAD; that is, changes in coronary risk factors would not be expected to produce immediate improvements in atherosclerotic plaque stability or coronary artery diameter (Clark et al., 2005). This is important because the essence of secondary prevention is, according to CACPR "[to] enhance adherence and compliance with long-term behaviours compatible with minimizing disease progression" (J. Stone et al., 2009). Knowledge users require evidence that demonstrates the long term effectiveness of interventions for risk reduction and CHD in order to justify time and resources that go into any SP intervention. In conclusion, the accuracy and precision of conclusions made in this review are limited by the variable quality of trials in our review.

### 4.1.3 Inconsistent Comparisons

The inconsistency of outcome measurements and control comparisons in our identified trials inhibited our abilities to make conclusions about these data. Of the 17 trials we evaluated, there was inconsistency in endpoints (refer to Table 1). As well, CBT-based interventions were compared to a wide variety of controls, making secondary analysis very difficult; comparing a CBT-based intervention to usual care, that does by definition not target cardiac risk factors, will plainly exhibit very different outcomes than when it is compared to traditional and comprehensive CR that addresses a number of risk factors. CBT-based interventions themselves were also diverse, being either single or multi-modality, addressing a range of risk factors, and being variable in duration and frequency as well as provider (refer to Table 1). Though European, American and Canadian guidelines on cardiac rehabilitation are similar (Balady et al., 2011; Grace et al., 2011; Kwan & Balady, 2012; Perk et al., 2012), according to our results, the evaluation of program effectiveness remains unpredictable. This is despite the existence of evidence-based secondary prevention quality indicators (Grace & Somanader, 2014). The

reasons for this are numerous; a lack of funding for long term program implementation and continued evaluation might be influential. We recommend that researchers, program developers and clinicians who facilitate SP for patients with CHD are better supported to coordinate and collaborate to access the evidence based guidelines and iteratively evaluate program effectiveness consistently.

## 4.2 Implications

This is the first systematic review and meta-analysis to document the added value that CBT has in secondary prevention of CHD. CBT has significant benefits in terms of improving depression and stress outcomes, and potential risk reduction in all-cause mortality and cardiovascular morbidity. CBT is at least as effective as traditional CR programs in terms of cardiovascular morbidity, all-cause mortality, anxiety, quality of life (QOL), and reductions in systolic blood pressure and total cholesterol.

### 4.2.1 Implications of Reducing Depression

Although the effectiveness of traditional CR for secondary prevention of CHD is well-established, recent research has found some deficiencies in traditional CR (Sandesara et al., 2015). Reported deficiencies include concerns around accessibility- particularly for minority and non-urban patients- cost, and an inability to effect long-term change on certain risk factors, in particular depression (Sandesara et al., 2015). Depression is relatively common in patients with coronary heart disease; in patients who have had myocardial infarction, depression rates are between 20-30% (Ski & Thompson, 2011). More broadly, patients with CHD are three times more likely to develop depression than the general population, and close to 20% of them meet criteria for major depression (Lichtman et al., 2009). The independent predictive effects of

depression on mortality is well documented, and when depression accompanies CHD, disease burden is inevitably amplified (Ski & Thompson, 2011). Within the CHD population, mild, moderate and major depression have been associated with a three to four fold higher risk of consequent cardiovascular morbidity and mortality (Ski & Thompson, 2011). In conjunction with chronic conditions such as CHD, major depression increases the frequency of healthcare and emergency department visits; the number of days lost due to illness; and worsens functional disability, all of which are linked with increased economic costs (Ski & Thompson, 2011). Depression is also linked to earlier and more severe cardiac events after an acute MI, as well as medical non-adherence, poor success rates in modifying cardiac risk factors, and a reduced quality of life (Ski & Thompson, 2011). Because of this, increased attention has focused on the role of depression both as a predictor and a consequence of CHD, especially myocardial infarction (Ragulies, 2002). An ongoing academic debate considers the benefits of screening for depression in all patients with CHD, illustrating the impact that depression has on outcomes in this population (Ski & Thompson, 2011). Regardless of the outcomes of this debate, our results are promising; the reduction in depression that we found that CBT-based interventions has over alternative methods therefore has implications for in terms of improvements in risk reduction, quality of life and potential cost effectiveness.

CBT-based interventions are at least equal to comprehensive cardiac rehabilitation (CR) in terms outcomes other than depression as well. This is congruent with previous evidence, the effectiveness of CBT for a variety of chronic illnesses is well established, and its benefits may exceed what is known (Moore et al., 2007; O'Neil et al., 2011). Cost-effectiveness data for CBT-based interventions specifically for SP of CHD is limited, although in two separate reports, Taylor et al. (2007) and Graham (2002) endorsed the Heart Manual as a cost-effective modality

when compared to hospital-based care. A 2010 cost-analysis study compared CBT to general practitioner (GP) care for treating depression in patients of all ages, and found that patients receiving only GP care recorded more GP consultations, greater use of antidepressants, and more psychiatric referrals (Moore et al., 2006). Brief outpatient CBT interventions have been shown to produce an immediate and sustained reduction in hospital admission costs for patients with angina (Moore et al., 2006). In addition, the flexibility of CBT means that services can be provided in virtually any setting and by a variety of providers. Our review findings support this, as we found no differences in outcomes between any of the above.

### 4.2.2 Better Description of Complex Interventions

Healthcare is a complex and adaptive system, with complex interventions (Glouberman & Zimmermann, 2002). Complexity refers to the interaction of many factors (REF). Superficial evaluations of complex interventions have limited application to present situations, and 'similar' past experiences may be poor predictors of future successes (Clark, Briffa, Thirsk, Neubeck, & Redfern, 2012). In order to be able to translate the abundance of research into clinical practice and programs, all components and complexities need to be better described. In our review, some of the trials included supplemental publications that provided descriptions of the interventions, but even these focused on the more easily described components (Clark, Briffa, et al., 2012). Current research on complex interventions that focuses on description of few mechanisms risks overlooking what really matters: which program components worked best for which patients, and when (Clark, Briffa, et al., 2012)?

In our review, most trials did provide basic information on provider, length of program, frequency of intervention, setting and modifiable risk factors addressed. Theoretical background

for the intervention was commonly missing. There are in fact a myriad of factors involved, including values, skills, and practices of the healthcare professionals providing the intervention; geographical, organisational, and socio-economical contexts in which the intervention is provided; interactions between contexts, and unpredictable factors ( Clark, Briffa, et al., 2012). Approaches that consider the complexity of these interventions would help explain outcomes better so that more can be learnt from failure, and thus improve the quality, usefulness, and translation of research into practice (Clark, Briffa, et al., 2012). For this reason, program description via an established taxonomy is warranted (Clark, 2013a).

The development, implementation and sustainability of SP interventions in healthcare climates concerned with cost-effectiveness and utility, necessitates consideration of these variables. Traditional methods of providing CR are costly and may miss opportunities to target real and long term behaviour change in patients with chronic CHD (Sandesara et al., 2015). Attendance and cost of traditional CR is also an issue (Sandesara et al., 2015). CBT interventions have the potential to ameliorate these concerns due to their flexibility and simple nature (Lewin et al., 2002). CBT can be provided at home or in hospital, in groups or for individuals and with a single practitioner of any discipline (Lewin et al., 2002).

### 4.2.3 Developing a Useful Evidence Base

Despite the existence of guidelines for cardiac rehabilitation for over 20 years, around 60%–70% of patients do not receive optimal secondary prevention for CHD (Clark, Redfern, & Briffa, 2014). Numerous trials and meta-analyses support the general success and quality of SP interventions of various duration, formats, and settings. Recent trial findings have led to questions about the value of supporting traditional centre-based CR in healthcare organizations

increasingly concerned with cost-effectiveness; though disagreement exists over whether these findings reflect true effects, confounded interventions or methodological weaknesses. Skepticism over the benefits of these interventions is not new —anecdotally multi-disciplinary providers have consistently expressed concerns around the sustainability of behavioural change from time-limited CR for patients with CHD (Clark et al., 2014). Unfortunately, mounting questions around *which* intervention components are most effective distracts from the principal aims of these programs; we, as researchers and healthcare providers are charged with ensuring that the greatest proportion of CHD patients are able to access and receive opportunities for behavior change and risk reduction.

Findings from this review shed some additional light on which components of SP interventions for CHD are successful. At minimum, we have determined that CBT-based interventions are desirable for reducing depression in patients with CHD, adding to the growing body of specific evidence on which program components are most effective for which patients. Our findings provide evidence for all knowledge users who design, plan and implement these programs, patients who can be motivated to participate and providers who can know they are improving their patients' health.

### 4.3 Limitations

As with all systematic reviews, our study has some limitations. Our interpretations were limited by the variable quality of the trials we included. Conclusions were also moderated by the heterogeneity of the reported outcomes, control comparisons, as well as clinical heterogeneity in terms of the design of the CBT interventions. We made several interpretation decisions that perhaps would have been more accurate if trials compared homogenous interventions to similar controls. For example, due to the heterogeneity in measuring outcomes and reporting of trials

evaluating effectiveness of CBT, and the lack of supplementary data, we needed to use raw depression scores at follow up when perhaps the mean change score may have been more illuminating

The lack of ethnicity data leads to concerns surrounding regarding generalizability to non-white populations; the consistent overrepresentation of white populations is problematic in most published trials. We were able to find ethnicity data for only one randomized trial (Neil Schneiderman et al., 2004). Equally, women were well represented in our included trials; due to a purposive sampling of women, 46% of participants included in this review were female. The over-representation of males in RCT's has historically been problematic (Hoel et al., 2009), so this is encouraging. As CBT has been traditionally utilized to treat depression in the overall population, depressed patients may have been overrepresented in this review (n = 2676; 52.8%). Although perhaps limiting generalizability, this finding may be constructive as depressed patients in the CHD population may be in the greatest need of SP interventions.

In our review protocol, we initially intended to compare CBT-based SP interventions to traditional CR; only six of the 17 trials made this comparison. 7 trials compared CBT-based interventions to single modality risk factor reduction, and fewer trials compared CBT-based SP interventions to usual care, which most often meant no further risk factor management. The clear benefits of SP interventions for CHD are not an unknown, thus when compared to usual care only, the added benefit of CBT is difficult to isolate. Sub-group and sensitivity analysis did ameliorate these concerns somewhat, but more precise comparisons would have yielded more precise conclusions. Finally, we could not make suppositions on cost-effectiveness and economic effects of CBT-based interventions tested in these trials because of the paucity of long-term data.

### 4.4 Conclusion

We established that traditional cardiac rehabilitation (CR) offers no significant advantages over CBT in terms of the outcomes we were able to evaluate (depression, stress, anxiety, QOL, all-cause mortality, CV morbidity, BP and total cholesterol). As such, CBT is an acceptable substitute to traditional CR, which continues to have difficulties around attendance and attrition rates (Sandesara et al., 2015). Clinically, our findings are of significance because CBT as an intervention is relatively inexpensive, portable and flexible in terms of provider (Moore et al., 2006).

CBT-based interventions for SP of CHD were *more* effective than non-CBT based interventions in reducing depression in these patients. We know that depression is an independent predictor of poor health, and when depression and CHD co-exist poor prognostic effects are tripled or quadrupled (Ski & Thompson, 2011). In addition to worsening prognosis for patients with CHD, depression is the leading cause of disability in all patients and populations worldwide, and is a major contributor to the global burden of disease (World Health Organization, 2012). As healthcare professionals are increasingly appreciating a balance between *quality* of life (QOL) and quantity of life (Remmel, 2011), targeting SP interventions to improve factors that worsen QOL is imperative.

Although the optimal design of the CBT-based intervention remains unclear due to inadequate intervention description, CBT-based programs may also improve other quality of life factors including stress and anxiety. We identified encouraging trends towards reduced risk of mortality, cardiovascular morbidity and stress through CBT-based interventions for the CHD population. While the flexibility of CBT-based interventions have the potential to reduce health care resource use (Furze et al., 2008), effectiveness of all program components as well as cost-

effectiveness of CBT-based programs when compared to others has not been well evaluated thus far.

So, while the development and use of CBT-based SP interventions is defensible, higher quality and more usable evidence is necessary to inspire use of that evidence towards real change. Future research should evaluate the effectiveness of SP interventions over longer periods of time, provide and describe these interventions in consistent ways, and make useful and consistent comparisons. Specifically for the evaluation of CBT-based interventions, future inquiry should directly compare these interventions to traditional CR, and report cost-effectiveness and long term data. Only through the development of high-quality evidence will the delivery of SP interventions to patients with CHD transition from a disjointed and fragmented state to an organized service across sectors that can be more readily integrated, systematized and individualized for patients.

# CHAPTER 5: CONCLUSION

### 5.1 Contribution to Nursing

Dr. A. M. Clark, the primary author's academic supervisor on this project, is collaborating with an international team to classify all publications of secondary prevention (SP) programs for coronary heart disease (CHD). The INSPECT team intends to then identify which types and components of programs are most effective, adding valuable data to past research and generating specific knowledge that is accurate and useful for knowledge users ( Clark, 2013a). As the sub-review outlined in this manuscript will supplement the larger INSPECT project, our results and subsequent publications have potential to inform policy and practice in the area of cardiac sciences. Previous reviews in which Dr. Clark and collaborators have been involved have been utilized by influential policy makers. For example, they have been used to guide practice in Canada, have informed international recommendations for the European Society of Cardiology and the American Heart Association North America (Clark, 2013a). The INSPECT team have also led commissioned meta-analyses in the field of CHD for knowledge users from Public Health Agency of Canada (Clark et al., 2010). The primary author of this manuscript and Dr. Clark, with guidance from the international INSPECT team, are currently working on a manuscript of the results of this review for submission and potential publication in a suitable Cardiology journal. Our results may contribute to the larger body of knowledge and practice guidelines for SP programs for CHD in Alberta, Canada and perhaps globally.

Changing healthcare environments and increasing ambiguity of Registered Nurses' roles within them makes multidisciplinary collaboration of central importance to our futures. Growing evidence demonstrates the value of multidisciplinary collaboration both in research and practice; continuing to develop research capacity in clinical nurses will support their role in both doing

and applying healthcare research. Thus, nursing research endeavors should be visible both for our peers and multidisciplinary colleagues.

The evidence from this systematic review has potential to inform development and delivery of evidence-based secondary prevention guidelines for CHD; operational, efficient and cost effective programs demand a team of professionals who are each able to work at what they do best, without role overlap. For this to happen, the findings of this systematic review must be made available for knowledge users of all professions. We are working towards this by: preparing a manuscript of results for publication, maintaining CACPR membership and aiming to present an abstract of results at the next annual CACPR conference. The primary author will be seeking to obtain license as a Nurse Practitioner in Alberta, and will remain in communication with the INSPECT team upon transitioning to the clinical environment. This will be achieved through maintaining a mentorship relationship with the second reviewer L. McLean who will be continuing her work with INSPECT, as well as sustaining other valuable relationships at the University of Alberta. With hope, opportunities for involvement in both clinical and academic environments will allow the primary author to maintain professional associations in both.

### 5.2 Final Conclusion

The aforementioned systematic review aimed to find, evaluate and draw conclusions from trials that measured the effectiveness of cognitive behavioural therapy (CBT) as an intervention for secondary prevention (SP) of coronary heart disease (CHD). We identified 17 unique RCTs that met inclusion criteria, and synthesized data from 16 of these. The CBT-based interventions tested in our included trials varied substantially, as did outcomes measured and comparison control groups. Despite this, we were able to conclude through meta-analysis that CBT-based SP programs significantly reduce depression in patients with CHD when compared to non-CBT

based interventions; we also noted promising trends towards reduced risk of mortality and cardiovascular morbidity in this population. Due to the trial heterogeneity, the optimal design of the intervention, particularly in terms of frequency and duration, remains unclear, but data synthesis suggests that CBT-based programs may also improve other quality of life factors including stress and anxiety in the CHD population. There was a paucity of long-term or cost-effectiveness data, thus we were unable to make conclusions on this.

Concerns around the inconsistency of outcome measurement, comparison control group, as well as general heterogeneity of the CBT intervention were barriers to meta-analysis and subsequent synthesis of clear and functional data for knowledge users. We therefore recommend that more consistent outcomes measurement be developed through guidelines, and utilized for measuring effectiveness of SP for CHD in general, and for CBT for SP of CHD specifically. Future research to evaluate cost-effectiveness of CBT through long-term follow up, and compared directly to traditional CR, would be beneficial.

The positioning of this review within the larger context of Dr. Clark et al.'s work on the INSPECT review adds both to the significance of this thesis, and has allowed the primary author opportunities for additional valuable research experience (Clark, 2013a). This thesis is an important beginning step towards both an academic and clinical career. There is noteworthy potential for future involvement in continued research, knowledge translation, policy development, and practice improvement in the field of SP of CHD. "Knowledge must be of something which is, as ignorance is of something which is not; and there is a third thing, which both is and is not, and is matter of opinion only" (Rosen, 2005, p. 354). The value of knowledge and earned experience is fundamental to an illustrious and rewarding career in nursing.

# Appendices

*Appendix A:* Search Strategy

| Database | Platform | Date search run | # of citations retrieved |
|---|---|---|---|
| MEDLINE 1946- | Ovid | 10 Feb 2014 | 112 |
| MEDLINE In-Process and Other Non-Indexed Citations | Ovid | 10 Feb 2014 | 1 |
| Embase 1988- | Ovid | 10 Feb 2014 | 213 |
| PsycINFO 1987- | Ovid | 10 Feb 2014 | 133 |
| EBM Reviews-Cochrane Central Register of Controlled Trials | Ovid | 10 Feb 2014 | 80 |
| CINAHL | EBSCOhost | 10 Feb 2014 | 93 |
| Web of Science: Science Citation Index, Social Sciences Citation Index, Conference Proceedings Citation Index-Science, Conference Proceedings Citation Index-Social Science & Humanities, Book Citation Index-Science, Book Citation Index-Social Science | Web of Science | 10 Feb 2014 | 94 |
| Scopus 1960- | | 10 Feb 2014 | 646 |

Medline & Medline In-Process and Other Non-Indexed Citations

1. heart diseases/ or myocardial ischemia/ or acute coronary syndrome/ or angina pectoris/ or exp angina, unstable/ or coronary disease/ or coronary aneurysm/ or coronary artery disease/ or coronary occlusion/ or coronary stenosis/ or coronary thrombosis/ or myocardial infarction/

2. (coronary artery disease* or atherosclerotic heart disease* or Arteriosclerotic heart disease*).ti,ab.

3. (Acute coronary syndrome* or angina or heart attack or myocardial infarct* or heart infarct*).ti,ab.

4. ((Ischem* or ischaem*) adj3 (heart or cardio* or myocard* or coronary)).ti,ab.

5. ((coronary or heart) adj3 (aneurysm* or occlusion* or stenosis or thrombosis)).ti,ab.

6. or/1-5

7. cognitive therapy/ or "acceptance and commitment therapy"/ or mindfulness/

8. (cognitive behavioral therapy or behavior therapy or cognitive therapy).mp.

9. heart manual.mp.

10. or/7-9

11. 6 and 10

12. randomized controlled trial.pt.

13. clinical trial.pt.

14. randomi?ed.ti,ab.

15. placebo.ti,ab.

16. randomly.ti,ab.

17. trial.ti,ab.

18. or/12-17

19. animals/

20. 18 not 19

21. 11 and 20

22. limit 21 to (english language and yr="1995 -Current")

Embase

1. *heart disease/ or exp *heart aneurysm/ or exp *heart arrhythmia/ or exp *intracardiac thrombosis/ or exp *ischemic heart disease/ or exp *myocardial disease/ or exp *pericardial disease/ or exp *valvular heart disease/

2. (coronary artery disease* or atherosclerotic heart disease* or Arteriosclerotic heart disease*).ti,ab.

3. (Acute coronary syndrome* or angina or heart attack or myocardial infarct* or heart infarct*).ti,ab.

4. ((Ischem* or ischaem*) adj3 (heart or cardio* or myocard* or coronary)).ti,ab.

5. ((coronary or heart) adj3 (aneurysm* or occlusion* or stenosis or thrombosis)).ti,ab.

6. or/1-5

7. cognitive therapy/

8. (cognitive behavioral therapy or behavior therapy or cognitive therapy).mp.

9. heart manual.mp.

10. or/7-9

11. 6 and 10

13. exp clinical trial/

14. randomi?ed.ti,ab.

15. placebo.ti,ab.

16. randomly.ti,ab.

17. trial.ti,ab.

18. or/13-17

19. animal/

20. 18 not 19

21. 10 and 20

22. limit 21 to (english language and yr="1995 -Current")

PsycINFO

1. exp cardiovascular disorders/

2. (coronary artery disease* or atherosclerotic heart disease* or Arteriosclerotic heart disease*).mp.

3. (Acute coronary syndrome* or angina or heart attack or myocardial infarct* or heart infarct*).mp.

4. ((Ischem* or ischaem*) adj3 (heartor cardio* or myocard* or coronary)).mp.

5. ((coronary or heart) adj3 (aneurysm* or occlusion* or stenosis or thrombosis)).mp.

6. or/1-5

7. cognitive behavior therapy/ or exp behavior modification/ or exp behavior therapy/ or cognitive restructuring/ or cognitive therapy/

8. (cognitive behavioral therapy or behavior therapy or cognitive therapy).mp.

9. heart manual.mp.

10. or/7-9

11. 6 and 10

12. clinical trials/

13. randomi?ed.ti,ab.

14. placebo.ti,ab.

15. randomly.ti,ab.

16. trial.ti,ab.

17. or/12-16

18. 11 and 17

19. limit 18 to (english language and yr="1995 -Current")

EBMR

1. heart diseases/ or myocardial ischemia/ or acute coronary syndrome/ or angina pectoris/ or exp angina, unstable/ or coronary disease/ or coronary aneurysm/ or coronary artery disease/ or coronary occlusion/ or coronary stenosis/ or coronary thrombosis/ or myocardial infarction/

2. (coronary artery disease* or atherosclerotic heart disease* or Arteriosclerotic heart disease*).ti,ab.

3. (Acute coronary syndrome* or angina or heart attack or myocardial infarct* or heart infarct*).ti,ab.

4. ((Ischem* or ischaem*) adj3 (heart or cardio* or myocard* or coronary)).ti,ab.

5. ((coronary or heart) adj3 (aneurysm* or occlusion* or stenosis or thrombosis)).ti,ab.

6. or/1-5

7. cognitive therapy/ or "acceptance and commitment therapy"/ or mindfulness/

8. (cognitive behavioral therapy or behavior therapy or cognitive therapy).tw.

9. heart manual.tw.

10. or/7-9

11. 6 and 10

12. randomized controlled trial.pt.

13. clinical trial.pt.

14. randomi?ed.ti,ab.

15. placebo.ti,ab.

16. randomly.ti,ab.

17. trial.ti,ab.

18. or/12-17

19. animals/

20. 18 not 19

21. 11 and 20

22. limit 21 to (english language and yr="1995 -Current")

EbscoHost CINAHL

| | |
|---|---|
| | Limiters - English Language; Published Date: 19950101-20141231; Research Article |
| S20 | Search modes - Find all my search terms |
| S19 | S4 AND S8 AND S18 |
| S18 | S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 |
| S17 | (MH "Placebos") |
| S16 | TX placebo* |
| S15 | TX random* allocat* |
| S14 | (MH "Random Assignment") |
| S13 | TX "randomi* control* trial*" |
| S12 | TX ( (singl* n1 blind*) or (singl* n1 mask*) ) or TX ( (doubl* n1 blind*) or (doubl* n1 mask*) ) or TX ( (tripl* n1 blind*) or (tripl* n1 mask*) ) or TX ( (trebl* n1 blind*) or (trebl* n1 mask*) ) |
| S11 | TX clinic* n1 trial* |
| S10 | PT Clinical trial |
| S9 | (MH "Clinical Trials+") |
| S8 | S5 OR S6 OR S7 |

| | |
|---|---|
| S7 | "heart manual" |
| S6 | "cognitive behavioral therapy" or "behavior therapy" or "cognitive therapy" |
| S5 | (MH "Cognitive Therapy+") |
| S4 | S1 OR S2 OR S3 |
| S3 | ( (heart) N3 (aneurysm* or occlusion* or stenosis or thrombosis) ) OR ( (coronary) N3 (aneurysm* or occlusion* or stenosis or thrombosis) ) |
| S2 | ( "coronary artery disease*" or "atherosclerotic heart disease*" or "Arteriosclerotic heart disease*" ) OR ( "Acute coronary syndrome*" or angina or "heart attack" or "myocardial infarct*" or "heart infarct*" ) OR ( (ischaem*) N3 (heart or cardio* or myocard* or coronary) ) OR ( (ischem*) N3 (heart or cardio* or myocard* or coronary) ) |
| S1 | (MH "Heart Diseases") OR (MH "Arrhythmia+") OR (MH "Heart Arrest+") OR (MH "Myocardial Diseases+") OR (MH "Myocardial Ischemia+") OR (MH "Aneurysm+") OR (MH "Ischemia+") OR (MH "Hypertension+") OR (MH "Vascular Diseases") |

Web of Science

| | |
|---|---|
| #1 | TS=("coronary artery disease*" or "atherosclerotic heart disease*" or "Arteriosclerotic heart disease*" or "Acute coronary syndrome*" or angina or "heart attack" or "myocardial infarct*" or "heart infarct*") |
| #2 | TS=(ischaem* NEAR/3 heart) OR TS=(ischaem* NEAR/3 cardio*) OR TS=(ischaem* NEAR/3 myocard*) OR TS=(ischaem* NEAR/3 coronary) |
| #3 | TS=(ischem* NEAR/3 heart) OR TS=(ischem* NEAR/3 cardio*) OR TS=(ischem* NEAR/3 myocard*) OR TS=(ischem* NEAR/3 coronary) |
| #4 | TS=(coronary NEAR/3 aneurysm*) OR TS=(coronary NEAR/3 occlusion*) OR TS=(coronary NEAR/3 stenosis) OR TS=(coronary NEAR/3 thrombosis) |
| #5 | #1 OR #2 OR #3 OR #4 |
| #6 | TS=("cognitive behavioral therapy" or "behavior therapy" or "cognitive |

therapy")

#7 #5 AND #7

#8 (TS=("clinical trial" OR random* OR trial* OR placebo or "control trial")) AND LANGUAGE: (English) Timespan=1995-2014

#9 #7 AND #8

Scopus

(((TITLE-ABS-KEY("heart disease" OR "coronary disease" OR "Acute coronary syndrome*" OR angina OR "heart attack" OR "myocardial infarct*" OR "heart infarct*") OR TITLE-ABS-KEY(ischaem*) OR TITLE-ABS-KEY(ischem*)) AND PUBYEAR > 1994) AND (TITLE-ABS-KEY("cognitive behavioral therapy" OR "behavior therapy" OR "cognitive therapy"))) AND (TITLE-ABS-KEY("clinical trial" OR "controlled trial" OR random* OR "single blind*" OR "double blind*" OR "triple blind*" OR placebo))

# References

Balady, G. J., Ades, P. A., Bittner, V. A., Franklin, B. A., Gordon, N. F., Thomas, R. J., Tomaselli, G. F. and Yancy, C. W. (2011). Referral, enrollment, and delivery of cardiac rehabilitation/secondary prevention programs at clinical centers and beyond a presidential advisory from the American Heart Association. *Circulation, 124*(25), 2951-2960.

Barley, E. A., Walters, P., Haddad, M., Phillips, R., Achilla, E., McCrone, P., Van Marwijk, H., Mann, A., and Tylee, A. (2014). The UPBEAT Nurse-Delivered Personalized Care Intervention for People with Coronary Heart Disease Who Report Current Chest Pain and Depression: A Randomised Controlled Pilot Study. *PLoS ONE, 9*(6), 1-14. doi:10.1371/journal.pone.0098704

Bekke-Hansen, S., Trockel, M., Burg, M. M., and Taylor, C. B. (2012). Depressive symptom dimensions and cardiac prognosis following myocardial infarction: results from the ENRICHD clinical trial. *Psychological Medicine, 42*(1), 51-60.

Berkman, L. F., Blumenthal, J., Burg, M., Carney, R. M., Catellier, D., Cowan, M. J., Czajkowski, S.M., DeBusk, R., Hosking, J., Jaffe, A., Kaufmann, P.G., Mitchell, P., Norman, J., Powell, L.H., Raczynski, J.M. and Schneiderman, N. (2003). Effects of treating depression and low perceived social support on clinical events after myocardial infarction: The Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) randomized trial. *JAMA: Journal of the American Medical Association, 289*, 3106-3116. doi: http://dx.doi.org/10.1001/jama.289.23.3106

Berkman, L., Jaffe, A., Carney, R., Czajkowski, S., Kaufman, P., Blumenthal, J. A., Arias, P., Babyak, M., Baldewicz, T., Barefoot, J., Bennett, J., Carels, R., Crenshaw, B., Curtis, S., Davis, L., Fath, K., Forman, L., Hassett, A., et al. (ENRICHD investigators) (2001). Enhancing recovery in coronary heart disease (ENRICHD) study intervention: Rationale and design. *Psychosomatic Medicine, 63*(5), 747-755.

Bisoendial, R. J., Kastelein, J. P. J., and Stroes, E. S. G. (2007). C-reactive protein and atherogenesis: From fatty streak to clinical event. *Atherosclerosis, 195*.

Blom, M., Georgiades, A., Janszky, I., Alinaghizadeh, H., Lindvall, B., and Ahnve, S. (2009). Daily stress and social support among women with CAD: results from a 1-year randomized controlled stress management intervention study. *International Journal of Behavioral Medicine, 16*, 227-235.

Borenstein, M., Hedges, L. V., Higgins, J. P. T., and Rothstein, H. R. (2009). *Introduction to Meta-Analysis*. West Sussex, UK: John Wiley and Sons Ltd.

Burell, G., and Granlund, B. (2002). Women's Hearts Need Special Treatment. *International Journal of Behavioral Medicine, 9*(3), 228-242.

Button, K. S., Ioannidis, J. P. A., Mokrysz, C., Nosek, B. A., Flint, J., Robinson, E. S. J., and Munafo, M. R. (2013). Power failure: why small sample size undermines the reliability of neuroscience. *Nat Rev Neurosci, 14*(5), 365-376. doi:10.1038/nrn3475

Canadian Institute of Health Research (2012). Gender, Sex and Health Research Guide: A Tool for CIHR Applicants (2012 ed.): Canadian Institute of Health Research.

Canadian Nurses Association (2013). W*hy we are worried: the facts; Cardiovascular and cerebrovascular diseases*. Retrieved November, 2013, from http://www.cna-aiic.ca/sitecore%20modules/web/~/media/cna/files/en/fact_sheet_19_e.pdf

Carney, R. M., Blumenthal, J. A., Freedland, K. E., Youngblood, M., Veith, R. C., Burg, M. M., Cornell, C., Saab, P. G., Kaufmann, P. G., Czajkowski, S., and Jaffe, A. S. (ENRICHD Investigators) (2004). Depression and late mortality after myocardial infarction in the Enhancing Recovery in Coronary Heart Disease (ENRICHD) study. *Psychosomatic Medicine, 66*, 466-474. doi:http://dx.doi.org/10.1097/01.psy.0000133362.75075.a6

Carney, R. M., Freedland, K. E., Stein, P. K., Skala, J. A., Hoffman, P., and Jaffe, A. S. (2000). Change in heart rate and heart rate variability during treatment for depression in patients with coronary heart disease. *Psychosomatic Medicine, 62*(5), 639-647.

CRD (2009). Systematic Reviews: CRD's guidance for undertaking reviews in health care. CRD. Retrieved November, 2014, from http://www.york.ac.uk/inst/crd/pdf/Systematic_Reviews.pdf

Claesson, M., Birgander, L. S., Lindahl, B., Nasic, S., Astrom, M., Asplund, K., and Burell, G. (2005). Women's hearts - Stress management for women with ischemic heart disease: Explanatory analyses of a randomized controlled trial. *Journal of Cardiopulmonary Rehabilitation, 25*(2), 93-102.

Clark, A. M. (2013a). CHD Secondary prevention programs: Common and complex but poorly described. CIHR Knowledge Synthesis. (Unpublished grant proposal). University of Alberta, Edmonton.

Clark, A. M. (2013b). What are the components of complex interventions in healthcare? Theorizing approaches to parts, powers and the whole intervention. *Social science and medicine, 93*(1), 185-193. doi:http://dx.doi.org/10.1016/j.socscimed.2012.03.035

Clark, A. M., Arthur, H. M., Oh, P., Stone, J. A., Briffa, T., Chambers, T., Choby, A. A., Neubeck, L., Redfern, J., Shiri, A. and Thirsk, L. M. (2013). What components matter most in secondary prevention interventions for coronary heart disease? Better data for better knowledge usage (KRS Knowledge Synthesis Grant). University of Alberta: Canadian Institute of Health Research.

Clark, A. M., Briffa, T., Thirsk, L., Neubeck, L., and Redfern, J. (2012). What football teaches us about researching complex health interventions? *British Medical Journal, 345*(1), e8316. doi:10.1136/bmj.e8316

Clark, A. M., Hartling, L., Vandermeer, B., and McAlister, F. A. (2005). Meta-Analysis: Secondary Prevention Programs for Patients with Coronary Artery Disease. *Annals of Internal Medicine, 143*(9), 659-672. doi:http://dx.doi.org/10.7326/0003-4819-143-9-200511010-00010

Clark, A. M., Haykowsky, M., Kryworuchko, J., MacClure, T., Scott, J., DesMeules, M., Luo, W., Liang, Y. and McAlister, F. A. (2010). A meta-analysis of randomized control trials of home-based secondary prevention programs for coronary artery disease. *European Journal of Cardiovascular Prevention and Rehabilitation, 17*(3), 261-270. doi:doi:http://dx.doi.org/10.1097/HJR.0b013e32833090ef

Clark, A. M., Redfern, J., and Briffa, T. (2014). Cardiac rehabilitation: fit to face the future? *Heart (British Cardiac Society), 100*(5), 355-356. doi:10.1136/heartjnl-2013-304407

Clark, A. M., Redfern, J., Thompson, J. R., and Briffa, T. (2012). More data, better data or improved evidence translation: What will improve cardiovascular outcomes? *International Journal of Cardiology, 155*(3), 347-349. doi:doi:http://dx.doi.org/10.1016/j.ijcard.2011.10.036

Clark, M., Kelly, T., and Deighan, C. (2011). A systematic review of the heart manual literature. *European Journal of Cardiovascular Nursing, 10*(1), 3-13. doi:10.1016/j.ejcnurse.2010.03.003

Columbia University (2000- Cited 2015 Mar 25). Comparison of Depression Identification after Acute Coronary Syndrome: Quality of Life and Cost Outcomes (CODIACSQoL) *Clinical Trials.gov*. Bethesda (MD): National Library of Medicine (US).

D'Agostino, R. B., Sr., Vasan, R. S., Pencina, M. J., Wolf, P. A., Cobain, M., Massaro, J. M., and Kannel, W. B. (2008). General cardiovascular risk profile for use in primary care: the Framingham Heart Study. *Circulation, 117*(6), 743-753. doi:10.1161/circulationaha.107.699579

Dalal, H. M., Evans, P. H., Campbell, J. L., Taylor, R. S., Watt, A., Read, K. L. Q., Mourant, A. J., Wingham, J., Thompson, D. R. and Gray, D. J. (2007). Home-based versus hospital-based rehabilitation after myocardial infarction: A randomized trial with preference arms--Cornwall Heart Attack Rehabilitation Management Study (CHARMS). *International Journal of Cardiology, 119*(2), 202-211.

Dalal, H. M., Zawada, A., Jolly, K., Moxham, T., and Taylor, R. S. (2010). Home based versus centre based cardiac rehabilitation: Cochrane systematic review and meta-analysis. *BMJ (Online), 340*(7740), 249. doi:http://dx.doi.org/10.1136/bmj.b5631

De Feo, S., Tramarin, R., Ambrosetti, M., Riccio, C., Temporelli, P. L., Favretto, G., Furgi, G. and Griffo, R. (2012). Gender differences in cardiac rehabilitation programs from the Italian survey on cardiac rehabilitation (ISYDE-2008). *International Journal of Cardiology, 160*(2), 133-139. doi:http://dx.doi.org.login.ezproxy.library.ualberta.ca/10.1016/j.ijcard.2011.04.011

Doering, L. V., Cross, R., Vredevoe, D., Martinez-Maza, O., and Cowan, M. J. (2007). Infection, depression and immunity in women after coronary artery bypass: a pilot study of cognitive behavioural therapy. *Alternative Therapies in Health and Medicine, 13*(3), 18-21.

Fernandez, R. S., Davidson, P., Griffiths, R., Juergens, C., Stafford, B., and Salamonson, Y. (2009). A pilot randomised controlled trial comparing a health-related lifestyle self-management intervention with standard cardiac rehabilitation following an acute cardiac event: implications for a larger clinical trial. *Australian Critical Care, 22*(1), 17-27. doi:10.1016/j.aucc.2008.10.003

Freedland, K. E., Skala, J. A., Carney, R. M., Rubin, E. H., Lustman, P. J., Davila-Roman, V. G., Steinmeyer, B. C. and Hogue, C. W. (2009). Treatment of depression after coronary artery bypass surgery: a randomized controlled trial. *Archives of General Psychiatry, 66*(4), 387-396.

Furze, G., Cox, H., Morton, V., Chuang, L., Lewin, R. J. P., Nelson, P., Carty, R., Norris, H., Patel, N. and Elton, P. (2012). Randomized controlled trial of a lay-facilitated angina management programme. *Journal of Advanced Nursing, 68*, 2267-2279. doi:http://dx.doi.org/10.1111/j.1365-2648.2011.05920.x

Furze, G., Donnison, J., and Lewin, R. J. P. (2008). *The clinician's guide to chronic disease management for long-term conditions [electronic resource]: a cognitive-behavioural approach.* Keswick: M and K Update.

Gidron, Y., Davidson, K., and Bata, I. (1999). The short-term effects of a hostility-reduction intervention on male coronary heart disease patients. *Health Psychology, 18*(4), 416-420.

Glasziou, P., Chalmers, I., Altman, D. G., Bastian, H., Boutron, I., Brice, A., Jamtveldt, G., Farmer, A., Gersi, D., Groves, T., Heneghan, C., Hill, S., Lewin, S., Michie, S., Perera, R., Pomeroy, V., Tilson, J., Sheppard, S. and Williams, J. W. (2010). Taking healthcare interventions from trial to practice. *British Medical Association, 7769.* 384.

Glouberman, S., and Zimmermann, B. (2002). *Complicated and complex systems: what would successful reform of medicare look like?* Government of Canada Retrieved from http://publications.gc.ca.login.ezproxy.library.ualberta.ca/site/eng/235920/publication.html.

Grace, S. L., and Somanader, D. (2014). Using the Pan-Canadian Cardiac Rehabilitation and Secondary Prevention Quality Indicators in Practice: What are we Learning? *Current Issues and Trends in Cardiovascular Disease Prevention and Rehabilitation (CV Edge),* 7, 1-5.

Grace, S. L., Chessex, C., Arthur, H., Chan, S., Cyr, C., Dafoe, W., Juneau, M., Oh, P. and Suskin, N. (2011). Society position statement: Systematizing Inpatient Referral to Cardiac Rehabilitation 2010: Canadian Association of Cardiac Rehabilitation and Canadian Cardiovascular Society Joint Position Paper. Endorsed by the Cardiac Care Network of Ontario. *Canadian Journal of Cardiology, 27*, 192-199. doi:10.1016/j.cjca.2010.12.007

Gulliksson, M., Burell, G., Wessby, B., Lundin, L., Toss, H., and Svardsudd, K. (2011). Randomized controlled trial of cognitive behavioral therapy vs standard treatment to prevent recurrent cardiovascular events in patients with coronary heart disease. *European Heart Journal, 32*, 390. doi:http://dx.doi.org/10.1093/eurheartj/ehr323

Halford, J., and Brown, T. (2009). Cognitive-behavioural therapy as an adjunctive treatment in chronic physical illness. *Advances in Psychiatric Treatment, 15*(4), 306.

Hansson, G. K. (2009). Atherosclerosis-An immune disease: The Anitschkov Lecture 2007. *Atherosclerosis, 202*, 2-10.

Heart and Stroke Foundation (2012). Heart Disease Prevention. Retrieved March, 2015, from http://www.heartandstroke.com/site/c.ikIQLcMWJtE/b.3483919/k.EB14/Heart_disease__Prevention_and_risk_factors.htm

Higgins, J., and Green, C. (2011). *Cochrane Handbook for Systematic Reviews of Interventions* Retrieved from www.cochrane-handbook.org.

Higgins, J., and Thompson, S. (2002). Quantifying heterogeneity in a meta-analysis. *Statistical Medicine, 21*(11), 1539-1558.

Higgins, J., Thompson, S., Deeks, J., and Altman, D. (2003). Measuring inconsistency in meta-analyses. *BMJ, 327*(7414), 557-560. doi:10.1136/bmj.327.7414.557

Hoel, A., Kayssi, A., Brahmanandam, S., Belkin, M., Conte, M., and Nguyen, L. (2009). Under-representation of women and ethnic minorities in vascular surgery randomized controlled trials. *Journal of Vascular Surgery, 50*(2), 349-354. doi:10.1016/j.jvs.2009.01.012

Hoffmann, T. C., Erueti, C., and Glasziou, P. P. (2013). Poor description of non-pharmacological interventions: analysis of consecutive sample of randomised trials. *British Medical Journal, 347*.

Hospital Italiano de Buenos Aires (2000 - Cited 2015 Mar 25). Healthy Habits Program for High Cardiovascular Risk Patients: Randomized Controlled Clinical Trial *ClinicalTrials.gov*. Bethesda, MA: National Library of Medicine.

Jadad, A. R., Moore, R. A., Carroll, D., Jenkinson, C., Reynolds, D. J., Gavaghan, D. J., and McQuay, H. J. (1996). Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Controlled Clinical Trials, 17*(1), 1-12.

Jolly, K., Lip, G., Taylor, R., Greenfield, S., Raftery, J., Mant, J., Lane, D., Jones, M., Lee, K. W. and Stevens, A. (2007). The Birmingham Rehabilitation Uptake Maximisation Study (BRUM). Home-based compared with hospital-based cardiac rehabilitation in a multi-ethnic population: cost-effectiveness and patient adherence. *Health technology assessment (Winchester, England), 11*, 1-118.

Koertge, J., Janszky, I., Sundin, O., Blom, M., Georgiades, A., Laszlo, K. D., Alinaghizadeh, H. Ahnve, S. (2008). Effects of a stress management program on vital exhaustion and depression in women with coronary heart disease: a randomized controlled intervention study. *Journal of Internal Medicine, 263*(3), 281-293.

Kunik, M. E., Veazey, C., Cully, J. A., Souchek, J., Graham, D. P., Hopko, D., Carter, R., Sharafkhaneh, A., Goepfert, E. J., Wray, N. and Stanley, M. A. (2008). COPD education and

cognitive behavioral therapy group treatment for clinically significant symptoms of depression and anxiety in COPD patients: a randomized controlled trial. *Psychological Medicine, 38(3)*, 385-396.

Kwan, G., and Balady, G. J. (2012). Cardiac Rehabilitation 2012 Advancing the Field through Emerging Science. *Circulation, 125*(7), E369-E373.

Lett, H. S., Blumenthal, J. A., Babyak, M. A., Catellier, D. J., Carney, R. M., Berkman, L. F., Burg, M. M., Mitchell, P., Jaffe, A. S. Schneiderman, N. (2007). Social support and prognosis in patients at increased psychosocial risk recovering from myocardial infarction. *Health Psychology: Official Journal of the Division of Health Psychology, American Psychological Association, 26*(4), 418-427.

Lewin, B., Robertson, I. H., Cay, E. L., Irving, J. B., and Campbell, M. (1992). Effects of self-help post-myocardial infarction rehabilitation on psychological adjustment and use of health services. *The Lancet* (8800), 1036.

Lewin, R. J. P., Furze, G., Robinson, J., Griffith, K., Wiseman, S., Pye, M., and Boyle, R. (2002). A randomised controlled trial of a self-management plan for patients with newly diagnosed angina. *British Journal of General Practice, 52*, 194-196+199-201.

Lewin, R. J., Furze, G., Robinson, J., Griffith, K., Wiseman, S., Pye, M., and Boyle, R. (2002). A randomised controlled trial of a self-management plan for patients with newly diagnosed angina. *British Journal of General Practice, 52*(476), 194-196.

Lopez, A. D., Mathers, C. D., Ezzati, M., Jamison, D. T., and Murray, C. J. L. (2006). Global and regional burden of disease and risk factors, 2001: systematic analysis of population health

Lustman, P. J., Griffith, L. S., Freedland, K. E., Kissel, S. S., and Clouse, R. E. (1998). Cognitive behavior therapy for depression in type 2 diabetes mellitus. A randomized, controlled trial. *Annals of Internal Medicine, 129*(8), 613-621. doi:10.1136/ebmh.2.2.50

Mathers, C., Boerma, T., and Ma Fat, D. (2004). The Global Burden of Disease 2004 update (pp. 1-133). Switzerland: Department of Health Statistics and Informatics in the Information, Evidence and Research Cluster of WHO.

Mendes De Leon, C. F., Czajkowski, S. M., Freedland, K. E., Bang, H., Powell, L. H., Wu, C.,Burg, M. M., DiLillo, V., Ironson, G., Krumholz, H. M., Mitchell, P. and Blumenthal, J. A. (2006). The effect of a psychosocial intervention and quality of life after acute myocardial infarction: The Enhancing Recovery in Coronary Heart Disease (ENRICHD) clinical trial. *Journal of Cardiopulmonary Rehabilitation, 26*(1), 9-15.

Microsoft. (2013). Microsoft Excel [computer software]. Redmond, Washington: Microsoft.

Moore, R. K., Groves, D. G., Bridson, J. D., Grayson, A. D., Wong, H., Leach, A., Lewin, R., and Chester, M. R. (2007). A brief cognitive-behavioral intervention reduces hospital admissions in refractory angina patients. *Journal of Pain and Symptom Management, 33*(3), 310-316.

Murphy, B. M., Worcester, M. U. C., Higgins, R. O., Elliott, P. C., Le Grande, M. R., Mitchell, F., Navaratnam, H., Turner, A., Grigg, L., Tatoulis, J. and Goble, A. J. (2013).

Reduction in 2-year recurrent risk score and improved behavioral outcomes after participation in the "beating heart problems" self-management program: Results of a randomized controlled trial. *Journal of Cardiopulmonary Rehabilitation and Prevention, 33*, 220-228.

Oh, P., Cyr, C., Grace, S. L., Naidoo, K., Shin, A., Strong, M., and Suskin, N. (2009). Program Models for Cardiac Rehabilitation. In C. A. o. C. Rehabilitation (Ed.), Guidelines for Cardiac Rehabilitation and Cardiovascular Disease Prevention: Translating Knowledge into Action (3rd ed.). Winnipeg, Manitoba. Retrieved from https://cacr.encryptedsecure2.com/resources/documents/CACR3rdEdGuidelinesTOCandChapterEditors.pdf.

O'Neil, A., Sanderson, K., Oldenburg, B., and Taylor, C. B. (2011). Impact of depression treatment on mental and physical health-related quality of life of cardiac patients: A meta-analysis. *Journal of Cardiopulmonary Rehabilitation and Prevention, 31*(3), 146-156.

Orth-Gomér, K., Schneiderman, N., Wang, H. X., Walldin, C., Blom, M., and Jernberg, T. (2009). Stress reduction prolongs life in women with coronary disease: The Stockholm women's intervention trial for coronary heart disease (SWITCHD). *Circulation: Cardiovascular Quality and Outcomes, 2*(1), 25-32.

Perk, J., De Backer, G., Gohlke, H., Graham, I., Reiner, Z., Verschuren, W. M., Albus, V., Benlian, P., Boysen, G., Cifkova, R., Deaton, C., Ebragim, S., Fisher, M., Germano, G., Hobbs, R., Hoes, A., Karadwniz, S., Mexxzani, A., Prescott, E., Ryden, L., Scherer, M., Syvanne, M., Reimer, W., Vrints, C., Wood, D., Zamarano, J. and Zannad, F. (2012). European Guidelines on

cardiovascular disease prevention in clinical practice (version 2012): The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). *European Journal of Preventive Cardiology, 19*(4), 585-667.

Petticrew, M., and Roberts, R. (2006). *Systematic Reviews in the Social Sciences: A Practical Guide* Oxford, UK: Blackwell Publishing Ltd.

Peyrot, M., and Rubin, R. R. (2007). Behavioral and psychosocial interventions in diabetes: a conceptual review. *Diabetes Care, 30*(10), 2433-2440.

Prinja, S., Gupta, N., and Verma, R. (2010). Censoring in Clinical Trials: Review of Survival Analysis Techniques. *Indian Journal of Community Medicine : Official Publication of Indian Association of Preventive & Social Medicine*, *35*(2), 217–221. doi:10.4103/0970-0218.66859

Prior, P. L., Francis, J., Reitav, J., and Stone, J. A. (2009). Behavioural, Psychological and Functional Issues in Cardiovascular Disease and Cardiac Rehabilitation. In J. A. Stone (Ed.), Canadian Guidelines for Cardiac Rehabilitation and Cardiovascular Disease Prevention. In J. A. Stone (Series Ed.) (3rd ed.).

Ragulies, R. (2002). Depression as a predictor for coronary heart disease. A review and meta-analysis. *American Journal of Preventative Medicine, 23*, 51-61. Retrieved from

Remmel, E. (2011). Quantity versus quality of life: when should we stop treating a terminal illness? *Living While Dieing*. Retrieved from: https://www.psychologytoday.com/blog/living-while-dying/201102/quantity-versus-quality-life

Reuters, T. (2014). EndNote for Windows (Version x7.3).

Rosen, S. (2005). *Plato's Republic. [electronic resource] : a study*: New Haven : Yale University Press, c2005.

Saab, P. G., Bang, H., Williams, R. B., Powell, L. H., Schneiderman, N., Thoresen, C., Burg, M., and Keefe, F. for the ENRICHD investigators (2009). The impact of cognitive behavioral group training on event-free survival in patients with myocardial infarction: the ENRICHD experience. *Journal of Psychosomatic Research, 67*(1), 45-56. doi:http://dx.doi.org/10.1016/j.jpsychores.2009.01.015

Schneiderman, N., Saab, P. G., Catellier, D. J., Powell, L. H., DeBusk, R. F., Williams, R. B., Carney, R. M., Raczynski, J., Cowan, M. J., Berkman, L. F., and Kaufmann, P. G. (for the ENRICHD investigators) (2004). Psychosocial treatment within sex by ethnicity subgroups in the Enhancing Recovery in Coronary Heart Disease clinical trial. *Psychosomatic Medicine, 66*, 475-483. doi:http://dx.doi.org/10.1097/01.psy.0000133217.96180.e8

Shea, B. J., Grimshaw, J. M., Wells, G. A., Boers, M., Andersson, N., Hamel, C., and Bouter, L. M. (2007). Development of AMSTAR: A measurement tool to assess the methodological quality of systematic reviews. *BMC Medical Research Methodology, 7*(10). doi:10.1186/1471-2288-7-10

Ski, C. F., and Thompson, D. R. (2011). Beyond the blues: the need for integrated care pathways. *European Journal of Cardiovascular Prevention and Rehabilitation: Official Journal of The European Society of Cardiology, Working Groups on Epidemiology and Prevention and Cardiac Rehabilitation and Exercise Physiology, 18*(2), 218-221. doi:10.1177/1741826710389409

Sterne, J. A. C., Gavaghan, D., and Egger, M. (2000). Original articles: Publication and related bias in meta-analysis. Power of statistical tests and prevalence in the literature. *Journal of Clinical Epidemiology, 53*, 1119-1129. doi:10.1016/S0895-4356(00)00242-0

Stone, J. A., Arthur, H. M., and Suskin, N. G. (2009). Introduction to Cardiac Rehabilitation. In J. A. Stone, H. M. Arthurs, and N. Suskin (Eds.), Canadian Guidelines for Cardiac Rehabilitation and Cardiovascular Disease Prevention (3rd ed.). Winnipeg, MB.

Stone, J., Clark, A., and Arena, R. (2009). Cardiac Rehabilitation as Chronic Disease Care. Canadian Guidelines for Cardiac Rehabilitation and Cardiovascular Disease Prevention: Translating Knowledge into Action (3rd ed.). Winnipeg, Manitoba: Canadian Association of Cardiac Rehabilitation. Retrieved from https://cacr.encryptedsecure2.com/resources/guidelines.cfm.

Taylor, R. S., Brown, A., Ebrahim, S., Jolliffe, J., Noorani, H., Rees, K., Skidmore, B., Stone, J. A., Thompson, D. R. and Oldridge, N. (2004). Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized trials. *American Journal of Medicine, 116*, 682-697.

Taylor, R. S., Watt, A., Dalal, H. M., Evans, P. H., Campbell, J. L., Read, K. L., Mourant, A. J., Wingham, J., Thompson, D. R. and Pereira Gray, D. J. (2007). Home-based cardiac rehabilitation versus hospital-based rehabilitation: a cost effectiveness analysis. *International Journal of Cardiology, 119*(2), 196-201.

The Cochrane Collaboration (2014). RevMan (Version 5.3).

Tisminetzky, M., Bray, B. C., Miozzo, R., Aupont, O., and McLaughlin, T. J. (2011). Identifying symptom profiles of depression and anxiety in patients with an acute coronary syndrome using latent class and latent transition analysis. *International Journal of Psychiatry in Medicine, 42*(2), 195-210.

Trockel, M., Burg, M., Jaffe, A., Barbour, K., and Taylor, C. B. (2008). Smoking Behavior Postmvocardial Infarction Among ENRICHD Trial Participants: Cognitive Behavior Therapy Intervention for Depression and Low Perceived Social Support Compared With Care as Usual. *Psychosomatic Medicine, 70*(8), 875-882. doi:10.1097/PSY.0b013e3181842897

Turner, A., Hambridge, J., Baker, A., Bowman, J., and McElduff, P. (2012). Randomised controlled trial of group cognitive behavioural therapy versus brief intervention for depression in cardiac patients. *Australian and New Zealand Journal of Psychiatry, 47*, 235-243. doi: 10.1177/0004867412460592

University of Bologna (2000- Cited 2015 Mar 25). Treatment of Depression in Acute Coronary Syndrome (ACS) Patients (TREATED-ACS) *ClincalTrials.gov*. Bethesda, MA: National Library of Medicine.

University of Edinburgh. (2000 - Cited 2015 Mar 25). Pilot Study of a Self-help Intervention for Depression in Patients with a Chronic Disease *ClinicalTrials.gov*. Bethesda, MA: National Library of Medicine.

University of Washington. (2000 - Cited 2015 Mar 25). Motivational Interviewing and Cognitive Behavioral Therapy-based Intervention for Cardiovascular Disease Prevention Amongst American Indians with Diabetic and Depressive Symptoms *ClinicalTrials.gov*. Bethesda, MA: National Library of Medicine.

University of York (2014). Health Sciences, Emeritus and honorary appointments: Bob Lewin. from http://www.york.ac.uk/healthsciences/our-staff/emeritus/bob-lewin/

Uppsala University (2000 - Cited 2015 Mar 25). Internet-based Cognitive Behavior Therapy after Myocardial Infarction (U-CARE: Heart) *ClinicalTrials.gov*. Bethesda, MA: National Library of Medicine.

Wenger, N. K. (2013). Efficacy of cardiac rehabilitation in patients with coronary heart disease. *UpToDate*. Retrieved from UpToDate website: http://www.uptodate.com/contents/efficacy-of-cardiac-rehabilitation-in-patients-with-coronary-heart-disease?source=search_resultandsearch=cardiac+rehabilitationandselectedTitle=3~37

Willson, R., and Branch, R. (2007). *Cognitive Behavioural Therapy for Dummies* (R. Chilvers, B. Kramer, S. Bell, and C. Holden Eds.). West Sussex, England: John Wiley and Sons, Ltd.

World Health Organization (2012). *Depression: Fact sheet [online]*. (369). Retrieved from http://www.who.int/mediacentre/factsheets/fs369/en/.

Ying, W., Lon, L., Kwang, L., Wei, C., and Tien, H. (2013). P16-02: The Development of a Cognitive-behavior Group Intervention Program to Reduce the Hostility Levels of Coronary Heart Disease Patients and Its Effect on Autonomic Nervous System Function. *Korean Psychological Society Conference, 2013*(2), 235.