Effectiveness of nurse-led clinics for patients with coronary heart disease

A systematic review and meta-analysis

Ainagul Alzhanova

A thesis submitted for the degree of

Master of Clinical Science

Adelaide Nursing School

Faculty of Health and Medical Sciences

The University of Adelaide

June 2022

Table of Contents

List of Figures

List of Tables

Abstract

Objective: Coronary heart disease (CHD) is a primary cause of cardiovascular disease and a critical public health concern with increased burden on health care. Nurse-led clinics (NLCs) can potentially contribute in providing effective secondary prevention in patients with CHD. This review aims to determine effectiveness of NLCs in managing patients with CHD compared to usual care. Nurse-led clinics offer a healthcare service that is staffed and coordinated primarily by registered nurses, advanced practice nurses and/or nurse practitioners. They provide specialised healthcare, comprising assessment and evaluation, counselling, education, empowerment, treatment and/or case management for a range of health conditions, including CHD.

Introduction: This review presents the best available evidence in relation to NLCs for patients with CHD by updating an existing systematic review (SR) published in 2010. There is a growing evidence base of clinical trials with novel care components in NLCs that have not yet been incorporated into any of the more recent reviews in this area, which are consequently now outdated and/or have addressed different patient populations. Hence, there is a clear need to update the existing SR.

Inclusion criteria: Randomised controlled trials examining patients aged 18 years and above with existing or newly diagnosed CHD such as angina pectoris and myocardial infarction were included in the review. The intervention is NLCs for cardiac patients, whereas usual care may be managed by medical practitioners such as General Practitioners (GPs) or specialists and any other non-nursing healthcare professional.

Methods: Databases of unpublished and published literature have been searched for the period January 2008 until February 2022. Methodological quality assessment, data extraction and synthesis were undertaken using the SR management tools available through the Joanna Briggs Institute (JBI-SUMARI) and Revman. Grading of Recommendations Assessment, Development and Evaluation (GRADE) was used to assess the quality of evidence.

Results: From 1390 records, 16 studies published between 2008 and 2022 were eligible for inclusion, in addition to the 13 studies from the previous review. Of the additional 16 studies,

five evaluated all-cause mortality, two investigated symptoms such as chest pain exacerbations, including those requiring medical treatment. Twelve trials measured changes in risk factors for cardiac patients, eight trials provided self-reported measurements of health behaviour, 6 studies investigated patients' compliance to the treatment. Ten trials provided self-reported measurements of quality of life for cardiac patients. Nurse-led clinics may slightly reduce all-cause mortality among cardiac patients in comparison to usual care at the 12 months follow-up (odds ratio (OR) of 0.78; 95% confidence interval (CI), 0.54-1.13, P=0.19). Attendance at NLCs may slightly reduce symptoms of chest pain in the long term (OR 0.81; 95% CI, 0.64-1.04; P=0.10). Mean systolic blood pressure (BP) in the medium term (6-11 months) was 10.96 mmHg lower in NLCs (95% CI -15.49, -6.43, P<0.00001). For diastolic BP in the medium term, the mean BP was 8.47 mmHg lower in NLCs (95% CI -13.83, -3.12, P=0.002). There is little or no difference between NLCs and usual care in the likelihood of improving depression and anxiety. Patient satisfaction and utilisation of health service were not synthesised due to limited data.

Conclusion: The evidence of this review suggests that NLCs may play a significant role in providing care to patients with CHD and may have similar or better effects on the prevention and treatment of CHD compared to usual care. The current analysis suggested a favourable effect of NLCs on mortality, chest pain, and some cardiac risk factors. However, transformations in health behaviours, compliance to medications and health-related quality of life were less evident. Nevertheless, NLCs should be considered for delivering care to patients with CHD and establishing specialised healthcare services in the community.

Keywords: cardiac; coronary heart disease; myocardial infarction; nurse-led; clinics.

Systematic review registration number: registration number in PROSPERO is CRD42020205270.

Declaration

I, Ainagul Alzhanova, certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint award of this degree.

I give permission for the digital version of my thesis to be made available on the web, via the University's digital research repository, the Library Search and also through web search engines, unless permission has been granted by the University to restrict access for a period of time.

I acknowledge the support I have received for my research through the provision of an Australian Government Research Training Program Scholarship.

1 July 2022

Acknowledgement

Foremost, I would like to express my deepest gratitude to my dear supervisors Dr. Tim Schultz, Dr. Verena Schadewaldt and Prof. Jeroen Hendriks for the continuous support of my research and Master of Clinical Science studies, for their immense knowledge, patience, perseverance, enthusiasm and motivation. Their ongoing guidance, comments and suggestions helped me to find clarity and focus throughout the research and writing of this thesis. I could not have imagined having better mentors and supervisors for my study. I would not have completed my studies without this truly international team of minds, expertise and knowledge from Australia, Germany, and the Netherlands that invaluably contributed to my thesis. My genuine respect to you all.

I would like to thank the University of Adelaide for giving me the opportunity to undertake this exciting journey of completing the Master of Clinical Science and assisting me in attending a few short courses that empowered me in writing my thesis.

I would like to thank Vikki Langton, Liaison Librarian, the University of Adelaide, for her advice on search strategy, using university library and databases and finding all the precious articles that were included in this research paper.

I would like to thank Steven Basford, MRes whose professional services were procured to provide proofreading and editorial advice. This advice was limited to Standard D (language and illustrations) and Standard E (completeness and consistency) of the Australian Standards for Editing Practice and the Vancouver referencing style guide.

Finally, I would like to thank my family for putting up with me the last four years and allowing me to isolate myself in my room while refining my thesis and supporting me spiritually.

Abbreviations

ACE-inhibitors	Angiotensin-converting enzyme inhibitors
AF	Atrial fibrillation
AHPRA	Australian Health Practitioner Regulation Agency
APN	Advanced Nurse Practitioner
BMI	Body mass index
BP	Blood pressure
CABG	Coronary artery bypass graft
CHD	Coronary heart disease
CI	Confidence Interval
CR	Cardiac rehabilitation
GP	General Practitioner
DALY	Disability Adjusted Life Years
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HDL-C	High-density lipoprotein cholesterol
HF	Heart failure
HRQoL	Health-related quality of life
JBI	Joanna Briggs Institute
JBI SUMARI	JBI System for the Unified Management, Assessment and Review of Information
LDL	Low-density lipoprotein cholesterol
LT	Long-term
MDT	Multidisciplinary team
MT	Medium-term
MI	Myocardium infarction
NLC	Nurse-led clinic
NP	Nurse Practitioner
OR	Odds ratio
PCI	Percutaneous coronary intervention
PICO	Population, intervention, comparison and outcomes
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyses
PROSPERO	Prospective Register of Systematic Reviews
RACGP	The Royal Australian College of General Practitioners
RCT	Randomised controlled studies
RN	Registered Nurse
SMD	Standardized mean difference
SOF	Summary of Findings
SR	Systematic review
ST	Short-term
TC	Total cholesterol
WHO	World Health Organisation

Chapter 1 Introduction

1.1 Overview

This thesis presents a full systematic review and meta-analysis on the 'Effectiveness of nurse-led clinics for patients with coronary heart disease', including the development of the protocol[1] published in PROSPERO (Prospective Register of Systematic Reviews) that guided the conduct of the review. The JBI approach for evidence synthesis was used as a method, as this is an update to a previous review.[2]

This updated review is important as it includes a large number of new studies, more than double compared to the original review, which allowed the inclusion of new outcomes such as mortality, and medication adherence.

This review is an update of an existing SR published in 2010.[2] Over time, new evidence has been generated, and therefore updating the previous review was undertaken to add value to the existing evidence.[3] This updated SR has been conducted in accordance with the JBI methodology for SRs of evidence synthesis.[4] There are a total of 29 publications included in this review, with 16[5 20] new studies comprising the period of 2008 to 2022 in addition to 13 studies[21 33] from the previous review from 2002 to 2008, highlighting a clear need for an updated review of new evidence. A methodological refinement to the previous review is the use of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) to assess the quality of evidence. A 'Summary of findings' table for the primary outcomes has been created using the GRADEPro tool.[34] A meta-analysis was conducted where possible, and the results were presented as forest plots.

1.2 Thesis Structure

The first chapter of this thesis presents a brief background to the literature on coronary heart disease (CHD) and nurse-led clinics (NLCs). The methodological basis for conducting SR and the researcher's experience in this area are also presented in chapter 1. The SR protocol is then provided in chapter 2 which outlines the rationale, hypothesis, and designed methods for conducting the review. Additionally, the research question and the aim of the review, the PICO (population, intervention, comparison and outcomes) model, inclusion and exclusion criteria, and the search strategy development are presented in Chapter 2. Since Chapter 2

is registered as a stand-alone publication in PROSPERO, it cannot be altered and therefore contains some repetition of information on the background to NLCs. The SR itself is presented in Chapter 3. The thesis concludes with Chapter 4, outlining a discussion of the results of the SR in relation to the Australian healthcare system and in terms of implications for practice and future research.

1.3 Background

Coronary heart disease is a complex and multifactorial disease of both the heart and blood vessels and includes angina pectoris, myocardial infarction (MI) and silent myocardial ischemia.[35] Coronary heart disease is considered a major cause of mortality and loss of Disability Adjusted Life Years (DALY) worldwide.[35,36] According to the Global Burden of Disease, 43% of all cardiovascular disease (CVD) deaths are associated with CHD.[36] A great part of this burden impacts low and middle-income countries which account for almost 7 million deaths and 129 million DALYs every year.[36] For example, MI survivors are at great risk of recurrent infarction with an annual mortality rate five to six times higher than the population without CHD.[36] The increase in mortality of CHD from the beginning of the twentieth century to 1960 was mainly caused by coronary atherosclerosis with subsequent CHD.[35] The upsurge was closely related to the increase in the smoking rate, unhealthy lifestyle and diet changes. Furthermore, the ability to detect acute myocardial infarction after the invention of the electrocardiogram increased the acknowledgement and diagnosis of CHD.[35]

Although the mortality for this condition has gradually declined over the last decades; it still causes about one-third of all deaths in people older than 35 years.[35] With that, there are significant financial implications as CHD is considered to be the costliest disease. Its burden includes direct healthcare costs and non-health informal service costs,[37] such as productivity loss, paid employment, and carer's leave taken by the patients' families. The economy bears the loss of productivity from the patients with CHD and family members providing care, while the government has to pay out incapacity welfare.[37]

The rapid surge in chronic diseases in the twentieth century has directed the focus of healthcare services worldwide on activities to promote disease prevention and self-management with a patient-centred approach.[38] Accordingly, the ageing population living in

the community with chronic diseases has imposed greater demands on healthcare[39] and necessitated the redesign and strengthening of primary care services and structures.[40] One aspect of restructuring health care services has included the expansion and reinforcement of primary care with a focus on establishing long-standing relationships between the primary care providers and patients, formulating shared care plans and delivering advanced access to services and coordinated care as well as new ways of communication among the primary care team, patients and their families.[40] The expansion of primary care inevitably stressed the physician workforce, and it readily became clear that physicians alone would not be sufficient as primary care providers to deliver the high demand of care.[40] Therefore, the nursing practice also advanced in accordance with the dynamic requirements of patients, communities and healthcare institutions.[39] Healthcare services also aim to keep the population out of hospitals in their communities, and NLCs established in the communities are ideally positioned to perform and act towards this aim.[41]

Nurse-led clinics were initially introduced in the mid-1970s. They became vibrant health care innovations offering accessible, high-quality, patient-centred care that aims at providing patient satisfaction while yielding outcomes as good as and frequently better than the usual care delivered by doctors in conventional primary care settings.[42] Nurse-led clinics originated in primary care and in 1978 were structured according to the World Health Organisation (WHO) into Primary Health Care models of service aiming to provide community-based, efficient, accessible, and affordable care.[41] However, NLCs can specialise in a wide range of clinical conditions like diabetes, rheumatoid arthritis and asthma in both hospital outpatient settings and primary care.[41] Evidence shows that NLCs have resulted in lower waiting time for patients, more time for the patient to provide comprehensive and holistic care, increased patient satisfaction, and providing patients with comprehensive education and guidance on disease self-management.[41]

Nurse-led clinics are staffed and managed by advanced nurse practitioners (APNs), nurse practitioners (NP) or registered nurses (RNs) with clinical training and further specialisation in a specific area.[42] With increasing autonomy in NLCs, the nurses may have the capacity to admit and discharge patients, as well as collaborate with other healthcare specialists, including physiotherapists, dieticians, social workers and other medical consultants.[43] Nurses in NLCs play a significant role in providing education and health promotion, explaining the

course of the disease to patients and their families and carers, engaging with patients to identify their needs and wishes, and aligning that with guideline recommendations to provide tailored care. Education also includes shared decision-making and encouragement to adherence to the treatment regimen and self-management focusing on risk factor reduction and lifestyle modification.[44] For CHD, this role includes describing the symptoms of MI or angina and distinguishing between those that require medication, treatment or re-admission to the hospital.[43] Monitoring the patients' condition is another essential role of a nurse in the clinic, which involves a thorough physical assessment and, if necessary, ordering tests and investigations.[43] Psychological support (taking note of patients' worries, listening to their fears and concerns and adequately addressing them)[43] is also a significant role of a nurse in the clinic, although it is not presented in all the literature.

1.4 Systematic Review Methodology

The aim of a SR is to synthesise the results of existing knowledge in a comprehensive and unbiased way using rigorous methods to answer the review question.[4] Systematic reviews summarise the diverse available sources of evidence and retrieve the global knowledge for individual clinicians for implementation into their practice and policy. Systematic reviews are conducted in a structured research procedure to ensure significant and trustworthy results.[4]

The results of SRs often have an impact on healthcare policies and decisions.[4] Therefore, ensuring the quality of a SR is essential and depends on adherence to rigorous methods that are utilised to reduce the risk of bias while conducting the review and are different from the conventional literature review.[4] It is important for reviewers to have proper training on review methodology, meta-analysis and processes. All the supervisors have practical knowledge and experience in SRs, while the student has undertaken training on SR methodology by the Cochrane Collaboration, as well as training on the GRADE approach on the certainty of evidence in SRs.

Systematic reviews are considered the highest level of evidence to inform current clinical practice, policy and future research activities. To minimise potential bias in the review process, standard methods and techniques have been developed by a number of international organisations, including the Cochrane Collaboration, the Campbell Collaboration and the JBI. This review has followed the approach of previous iterations[2,45]

and used the JBI approach. The SR process, recommended by JBI, provides essential steps, including the preparation of the protocol, formulating the review question and determining eligibility criteria, the search strategy and final outcomes.[4]

Systematic reviews can synthesise qualitative research, quantitative research or both (mixed methods reviews). The JBI provides guidance for qualitative, quantitative, and mixed methods reviews.[4] The choice of review type is determined by the SR question and the formulation of its essential components, such as the population, intervention, comparison and outcome (PICO).[46] The review question should be clearly outlined and clinically important.[47] Based on the research question of this review, a quantitative SR of effectiveness was regarded to be the most applicable review method to evaluate the outcomes of NLCs clinics for CHD patients.

Once the review question is finalised, the next phase is to outline the objectives in an *a priori* protocol describing the methods that will be utilised to direct the review process. The protocol outlines the methods of searching and appraising the literature, as well as extracting and synthesising the data.[46] Prospective protocol registration in the PROSPERO database helps to avoid duplication and promotes transparency.[48]

The JBI quantitative SRs may include three major study designs: experimental, quasi-experimental and observational. Randomised controlled trials are the most rigorous way of ascertaining the existence of a cause-effect relation between the intervention and the outcome.[49] Well-conducted RCTs reduce bias and random errors.[49]

Following the completion of the protocol, the conduct of the SR commences with the development and testing of the search strategy. The search strategy should be inclusive and comprehensive in a SR as it aims at finding all evidence available to answer the proposed question. The subsequent screening of the results of the search strategy, and assessment of the methodological quality of the full text of included studies, are best performed by two reviewers, with the results presented in figures (for example, a PRISMA flow diagram) and tables (for example, a table of the characteristic of included studies). These methods of presenting the results provide an inclusive picture of these phases of the SR and the data quality of included studies.[48]

Finally, data extraction and synthesis are carried out using specific data extraction tools and meta-analysis to statistically combine the results of multiple, similar studies.[4] Meta-analysis is a statistical analysis of the results from the individual studies combined to address the same question in order to integrate the findings and generate an overall estimate of the effect of the treatment.[50] It offers a logical framework to systematically synthesise similar results from comparable studies, and where possible, combine the effect, measure, and examine consistency of outcomes and clarify inconsistencies.[50]

1.5 Researcher's Experience in this Field

The researcher of this thesis is a registered nurse with a Postgraduate Diploma in Cardiovascular Care, currently working in the Cardio-Thoracic Unit at a large metropolitan public hospital in Adelaide, South Australia. Approximately 70% of the inpatient workload here are patients with CHD, including patients' post-MI and requiring elective or urgent surgery for coronary artery bypass graft or valve replacement. As this type of clinical work involves consistent peri-operative care and education, and emotional and psychological support, it is important for nurses to remain up-to-date with the best available evidence on improving health behaviours, quality of life and compliance to treatment. The results from this review will have relevance for all nurses working in similar healthcare settings, especially those who currently provide services in NLCs for patients with CHD or who may be interested in pursuing this in the future.

Chapter 2 Systematic Review Protocol

2.1 Introduction

Coronary heart disease is a primary cause of cardiovascular diseases and a critical public health concern with increased mortality among adults.[51] In 2012, worldwide mortality caused by CHD reached 7.2 million, and by 2020 it is expected to exceed 11.1 million,[52] representing a significant burden to healthcare and society. Over the course of the disease, patients may experience multiple re-hospitalisations with a cumulative burden on the healthcare system. Thus, it is important to evaluate the benefits of secondary preventive care for CHD.[53]

Coronary heart disease, such as angina pectoris and myocardial infarction, is a complex and multifactorial condition with variable treatment depending on the severity of the symptoms[54] and underlying co-morbidities. It is associated with a plaque build-up (atherosclerosis) inside the coronary arteries that supply oxygenated blood to the heart muscle.[55] The hardened or ruptured plaque can partially or completely obstruct the blood flow to the coronary artery causing chest pain and heart attack.[56] Patients with chronic CHD are very likely to have recurrent cardiac complications and mortality.[57] Coronary heart disease also impairs quality of life and hampers physical and social activities of patients.[58]

An unhealthy lifestyle considerably contributes to the development of cardiovascular risk factors and cardiac diseases. Therefore, preventive guidelines on cardiovascular disease include lifestyle education on physical exercise, smoking cessation, a healthy diet and alcohol consumption. The compliance with healthy lifestyle choices in a pre-clinical population varies from 20% to 90%; thus, enhancing adherence requires effective behaviour-change programs and interventions, including cognitive and social elements.[59] Coronary heart disease, being a chronic disease, involves careful medical management with numerous recommendations, including a healthy lifestyle and nutrition, moderate-intensity physical activities, pharmacological management as well as patient education to promote understanding and compliance with therapies and alter health behaviours and improve health conditions.[60,61]

In the past, the focus on managing chronic diseases such as CHD shifted from hospital to the community. Nurse-led clinics highlighting health promotion and education and actively

involving patients to contribute to their care have emerged in community health care.[62] Nurse-led clinics were initially presented as a measure to provide transitional specialised care that integrates case management, disease monitoring and home-based rehabilitation programme, and support after the acute stage of illness, as well as to incorporate acute care to the rehabilitative level.[63]

An NLC is a clinical practice of healthcare provision that includes a nurse, a patient and their family supported by a multidisciplinary team.[41] They are operated by specialised nurses for patients' support and generally focus on the management of a specific chronic disease.[41] Nurses, as primary caregivers, deliver care with respect to patients' values, needs and preferences as well as to the patients' disease experiences and knowledge, and encourages patients in their self-management and compliance to the therapeutic regimen. They are specially trained and equipped to provide patient-centred care for health promotion, prevention and maintenance of the disease.[58] The functioning of the NLCs involves collaboration within the multidisciplinary team, including doctors, dieticians, social workers and allied health.[63]

The main components of NLCs care include evaluation of healthcare needs, counselling, education, empowerment, treatment and case management. Nurse-led clinics enhance communication between patients and health professionals, taking into consideration individual values and disease progression, where nurses relate not only to patients' symptoms but also their psychosocial and cognitive background.[58] Unlike a general practice clinic focussing on medications, NLCs use a holistic approach in attending to the needs, values and preferences of patients and families based on comprehensive guidelines.[63]

Nurse-led clinics can potentially improve compliance and risk factor control and thereby provide effective secondary prevention in patients with CHD.[64] Effective secondary prevention of CHD can lead to reductions in the following patient outcomes: frequency of angina, myocardial infarction and even cardiac-related death. Randomised control studies have reported no harmful effects but rather positive influence on the quality of life and wellbeing in general.[65] The regular assessments of risk factors and counselling on lifestyle and health status provided by NLCs may constructively modify such important behaviours as diet and exercise, treatment/medication adherence and smoking cessation.

2.2 Update and Expansion of Existing Reviews

Several reviews of NLCs on cardiovascular diseases have recently been published. The study and meta-analysis by Al-Mallah et al.[66] suggested that NLCs reduce major adverse cardiac events and all-cause mortality for cardiovascular patients, including angina myocardial infarction. It appraised the effectiveness of NLCs in terms of morbidity and mortality of outpatients as well as lipid control and adherence to medications from trials up to 2013. In contrast to Al-Mallah's review, the present review will include telehealth care as an intervention as well as trials with a follow-up duration of less and more than 9 months to assess the short- and long-term efficacy of the clinics. Another review by Snaterse et al.[57] summarised the effective components of nurse-coordinated clinics in preventing recurring cardiac events and included trials from 1990 to January 2015. It demonstrated a positive effect on the outcomes such as monitoring blood pressure, control of cholesterol, and cessation of smoking. It included clinics with cardiac rehabilitation programs (CR) as an intervention, which will be excluded in the present review as the concept of CR considerably differs from one of the NLCs. The SR published on this topic in 2010 by Schadewaldt and Schultz[2], concluded that nurse-led care was equivalent to non-nurse-managed clinics, and there was no further risk of poorer outcomes in the NLCs.

Subsequently, many relevant studies have been published on NLCs since the three previous reviews were undertaken, and an update is therefore warranted. Therefore, the proposed study aims to update the existing review of NLCs for CHD by Schadewaldt and Schultz.[2] The updated study will identify and appraise the best existing evidence on the effectiveness of NLCs and their components for cardiac patients. The aim of this review has continuing importance to clinicians and decision-makers as well as for future clinical guidelines; new data and new evidence are available that may have a meaningful impact on the findings of the review. The update of the existing review gives an opportunity to review the eligibility criteria used in the review.

As an expansion to the previous review, other synonymous terms that refer to nurse-led care, prevention and health promotion, such as nurse-initiated, nurse-managed and nurse-coordinated clinics, will be used in this review.

2.3 Review Question

The research question for this review is:

What is the effectiveness of nurse-led clinics for patients with coronary heart disease on mortality and morbidity and other patient outcomes?

2.4 Inclusion Criteria

2.4.1 Population

Patients 18 years old and above with existing or newly diagnosed CHD such as angina pectoris symptoms and myocardial infarctions will be included in the review. Heart failure, cardiomyopathies, congenital heart diseases, arrhythmias, and other cardiovascular diseases such as stroke or peripheral vascular diseases will be excluded from the review. Studies in which patients with multiple diseases were enrolled will be included, provided the outcomes for patients with CHD are reported separately, or patients with CHD comprise at least 60% of the trial participants.

2.4.2 Intervention

The intervention is NLCs for cardiac patients. Nurse-led clinics provide specialised healthcare, comprising assessment and evaluation, counselling, education, empowerment, treatment and/or case management for a range of health conditions, including CHD. We define nurse-led clinics as staffed and coordinated primarily by registered nurses, advanced practice nurses and/or nurse practitioners. They deliver education, assessment, treatment and monitoring, consultation and referral to other health disciplines while collaborating with and potentially under the supervision of doctors and other healthcare professionals.

Nurse-led clinics for CHD patients deliver a range of secondary prevention programs on lifestyle changes, including weight reduction, increased physical activity, encouragement in smoking cessation and diet advice, telehealth education after discharge for better access and improved health outcomes, individual health education on risk management and treatment of risk management, initiated in the hospital and continued at home and through regular follow-ups. Nurse-led clinics provide training courses on self-management, behaviour change models and promotion of therapy adherence, potentially improving patient

compliance and controlling risk factors in cardiac patients. Ideally, patients are empowered in shared decision-making.

Studies that assessed rehabilitation programmes as an intervention will be excluded from this review. Although cardiac rehabilitation programs and NLCs for cardiac patients have similarities, there are obvious differences between them. CR uses a short-term model with the focus on increased physical fitness and physical activities and return to work for CVD patients,[67] with the provision of group sessions compared to one-to-one long-term care in NLC.[67]

2.4.3 Comparator

Non-nurse-led interventions will include those managed by medical practitioners such as GPs, specialists, or non-nursing healthcare professional.

2.4.4 Outcomes

The outcomes to be considered in this review are:

• All-cause mortality

• Exacerbations of heart disease symptoms or angina attacks requiring medical treatment (e.g., presentations to emergency department, readmission to hospital)

• Reduction of risk factors (e.g., smoking cessation, exercise behaviour, diet)

• Self-management (e.g., patients' ability to perform new health care behaviour and compliance (treatment adherence according to clinical guidance)

• Length of stay

• Health status and health-related quality of life (e.g. as measured by the Seattle Angina Questionnaire, Short Form Health Survey (SF-36) or Quality of Life Index – Cardiac Version III),[68] as well as mental health outcomes including depression and anxiety, which may be measured using the SF-36, Depression Anxiety Stress Scale (DASS 21), Beck Depression and Anxiety Inventories, Hospital Anxiety and Depression Scale (HADS) and other validated tools.[69]

• Patient satisfaction (as measured using valid tools, including the 'Treatment Satisfaction' domain of the Seattle Angina Questionnaire).[68]

• Utilization (e.g., number of consultations, length of consultation, prescriptions, tests and investigations, use of other services).

The outcomes maybe subdivided into short-, medium- and long-term interventions periods short- (0 to 6 months), medium- (7 to 11 months) and long-term (12+ months) follow-up time periods.

2.4.5 Types of studies

Randomised controlled trials (RCTs) will be included in this review of NLCs for CHD patients. Should both cluster-randomised trials and individually randomised trials be identified, the relevant information will be synthesised.

2.5 Methods

This review is an update of the existing review published in 2010 (Schadewaldt & Schultz)[2], which was conducted according to the JBI method. Databases of unpublished and published literature will be searched for the period January 2008 until the present, as the existing review's search ended in March 2008.

2.5.1 Search strategy

The search strategy aims to identify both published and unpublished trials. A preliminary basic search of PubMed and CINAHL was carried out to locate articles on the topic, followed by the analysis of the titles and abstracts of the relevant studies. A full search strategy for PubMed is presented in Appendix I. The reference list of all articles selected for critical appraisal will be scanned for additional studies.

2.5.2 Information sources

The following bibliographic databases will be used to identify trials through systematic searches:

• Cochrane Central Register of Controlled Trials (CENTRAL) on the Cochrane Library

• PubMed

• EMBASE (Ovid)

• PsycINFO (Ovid)

• Conference Proceedings Citation Index-S (CPCI-S) on Web of Science (Thomson Reuters)

• CINAHL (EBSCO)

• LILACS (Bireme)

The preliminary search strategy for PubMed will be adapted for use in the other databases.

2.5.3 Study selection

Following the search, all identified citations will be collated and uploaded into EndNote X9, and duplicates will be removed. At least two authors will independently screen titles and abstracts of all search results against the inclusion criteria. The full text of studies that may potentially meet the inclusion criteria will be retrieved, and the citation will be imported into JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI).[70] The full text of selected trials will be retrieved and assessed in detail against inclusion criteria independently by two authors. Ineligible studies that do not meet the criteria will be excluded, the reasons for which will be provided in an appendix in the final review report. Multiple publications on the same study will be included, provided relevant outcomes are presented. They will be considered as one study. If disagreements arise between the reviewers on inclusion, a third author will be involved to reach a consensus decision. The selection process and the results of the search will be outlined in a Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram.[71]

2.5.4 Assessment of methodological quality

Two independent reviewers will critically appraise the methodological quality of the selected study by applying standard critical appraisal instruments from the JBI.[72] Should disagreements emerge during the assessment process; they will be resolved through consultation or deploying a third reviewer. The results will be presented both in a table and

in a narrative form. The authors will undertake data extraction and synthesis of all studies, regardless of the results of their methodological quality.

2.5.5 Data extraction

Two authors will independently extract outcome data from included studies using the Review Manager. The primary reviewer will transfer the data into the Review Manager.[73] Any disagreements that arise between the reviewers will be resolved through discussion or with a third reviewer.

The following study characteristics will be included.

1. Methods: study design, total duration of the study, number of study centres and location, study setting, withdrawals, and date of the study.

2. Participants: number, mean age ± SD, age range, gender, the severity of the condition, diagnostic criteria, existing heart disease, inclusion criteria, and exclusion criteria.

3. Interventions: intervention, comparison.

4. Outcomes: primary and secondary outcomes specified and collected, and time points reported.

5. Notes: funding for the trial and notable conflicts of interest of the trial authors.

We will double-check that data are entered correctly by comparing the data presented in the SR with the study reports. A second review author will spot-check study characteristics for accuracy against the trial report.

Investigators of original studies will be contacted in order to verify key study characteristics that are unclear and/or obtain missing outcome data. Where this is not possible, and the missing data are thought to introduce serious bias, we will explore the impact of including such studies in the overall assessment of results by a sensitivity analysis.

2.5.6 Data synthesis

Data synthesis will be performed where possible using Revman.[73] Random-effects models will be used in meta-analyses. Results of both groups will be reported should there be discrepancies between results. Otherwise, the random-effects model results will be presented.

Meta-analyses will only be undertaken where this is meaningful, i.e., if the interventions, technologies, participants, and the underlying clinical questions are similar enough for pooling to make sense. A narrative summary of the data will be presented should it be not possible to do a meta-analysis. Dichotomous data will be analysed as odds ratios with 95% confidence intervals and continuous data as mean differences or standardised mean differences with 95% confidence intervals. Data will be presented as a scale with a consistent direction of effect. The I^2 statistic will be used to measure heterogeneity among the trials in each analysis.

Skewed data will be described as medians and interquartile ranges.

2.5.7 Sub-group analysis

If possible, a sub-group analysis on the intensity of the intervention, for example, a one-off education session compared to interventions that are delivered at regular intervals, will also be undertaken.

Other subgroup analyses for the primary outcomes will also be performed, using stratified meta-analysis, according to the following:

• Trials including patients with angina pectoris versus patients with myocardial infarction,

• Outcomes measured at a short follow-up period (less than six months) versus a longer follow-up period (six months or more),

• Trials reporting results for men versus women separately,

• Trials with cluster RCTs versus individual RCTs.

2.5.8 Sensitivity analysis

The following sensitivity analysis will be undertaken: a comparison of studies with a high risk of bias and a low risk of bias to check for consistency of results.

A funnel plot will be created for more than 10 trials to explore possible small study biases for the primary outcome.

2.5.9 Assessing certainty in the findings

The quality of evidence will be assessed according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) by creating a 'Summary of findings' table for the primary outcomes using the GRADEPro tool.[34] The following main outcomes will be reported in the 'Summary of findings table': outcomes related to the effectiveness of NLCs listed in this protocol. The quality of evidence will be based on the following criteria: methodological limitations, consistency and risk of bias.

2.6 Acknowledgements

This research will fulfil the requirements for the successful completion of the degree of the Master of Clinical Science program at the University of Adelaide, South Australia, for AA.

2.7 Funding

No funding was received to undertake the review.

2.8 Conflicts of Interest

The authors do not have any potential conflict of interest or any personal, professional or financial interests in this review project.

Appendix I: Search strategy

PubMed

Limitations:

Date: 1 January 2008 – 2020

Language: English

Coronary heart disease	Nurse led clinics	Randomised Controlled Trial
"Coronary Disease" [mh:noexp] OR "coronary artery diseases"[mh] OR "coronary occlusion"[mh] OR "coronary stenosis"[mh] OR "coronary heart disease*" [tiab] OR "coronary disease*" [tiab] OR "myocardial infarction" [tiab] OR "coronary artery disease*" [tiab] OR "coronary occlusion" [tiab] OR cardiac [tiab]	"Practice Patterns, Nurses'" [mh] OR "nurse coordinated clinic*" [tiab] OR "nurse led clinic*"[tiab] OR "Nurse initiated"[tiab] OR "Nurse managed"[TIAB] OR "nurse led"[tiab]	"Clinical stud*" [all] OR "Randomised Controlled Trial*"[all] OR "Clinical trial*" [all] OR "Controlled Clinical Trial*" [all] OR "randomi*[all] OR "randomly" [all] OR "RCT*"[all]

	Search strategy dated 21.04.2019	Records retrieved
S1	"coronary disease" [mh:noexp]	130069
S2	"coronary artery diseases" [mh]	0
S3	"coronary stenosis" [mh]	17817
S4	"coronary heart disease*" [tiab]	48387
S5	"coronary disease*"[tiab]	19478
S6	"myocardial infarction"[tiab]	173225
S7	"coronary artery disease*"[tiab]	82933
S8	"coronary occlusion"[tiab]	6181
S9	cardiac[tiab]	580490
S10	"Practice Patterns, Nurses'"[mh]	2421
S11	"nurse coordinated clinic*"[tiab]	0
S12	"nurse led clinic*"[tiab]	171
S13	"Nurse initiated"[tiab]	323
S14	"Nurse managed"[tiab]	534
S15	"nurse led"[tiab]	3424
S16	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9	870981
S17	S10 OR S11 OR S 12 OR S13 OR S14 OR S15	2421
S18	"Randomised Controlled Trial*"[all]	512175
S19	"Clinical stud*"[all]	0
S20	"Clinical trial*"[all]	691680
S21	"Controlled Clinical Trial*"[all]	105967
S22	randomi*[all]	843161
S23	"randomly"[all]	317856
S24	"RCT*"[all]	20504
S25	S18 OR S 19 OR S20 OR S21 OR S22 OR S23 OR S 24	1417252
S26	S16 AND S17 AND S25	158

Chapter 3 Systematic Review

3.1 Introduction

Coronary heart disease is a primary cause of cardiovascular diseases and a critical public health concern with increased mortality among adults.[51] In 2012, worldwide mortality caused by CHD reached 7.2 million, and by 2020 it was expected to exceed 11.1 million,[52] representing a significant burden to healthcare and society. Over the course of the disease, patients may experience multiple re-hospitalisations with a cumulative burden on the healthcare system; thus, it is important to evaluate the benefits of secondary preventive care for CHD.[53]

Coronary heart disease, such as angina pectoris and myocardial infarction, is a complex and multifactorial condition with variable treatment depending on the severity of the symptoms[54] and underlying co-morbidities. It is associated with a plaque build-up (atherosclerosis) inside the coronary arteries that supply oxygenated blood to the heart muscle.[55] The hardened or ruptured plaque can partially or completely obstruct the blood flow to the coronary artery causing chest pain and heart attack.[56] Patients with chronic CHD are very likely to have recurrent cardiac complications and are at a high risk of mortality.[57] Coronary heart disease also impairs quality of life and hampers physical and social activities of patients.[58]

The relationship between unhealthy lifestyle and the development of cardiovascular risk factors and cardiac diseases is well-established.[74] Therefore, preventive guidelines for CHD include education on lifestyle issues such as a healthy diet, physical exercise, smoking cessation and reduction of alcohol consumption[60] and promotion of understanding and compliance with therapies. The guidelines aim to alter health behaviours and improve health conditions.[61] The compliance with healthy lifestyle choices in a pre-clinical population varies from 20% to 90%; thus, enhancing adherence often requires effective behaviour-change programs and interventions, including cognitive and social elements.[59]

The focus on managing chronic diseases such as CHD has shifted from hospital settings to the community. This shift was accompanied by nurses playing a greater role in managing patient care. Nurse-led initiatives such as NLCs emerged in community health care.[75] Nurse-led clinics were initially presented as a measure to provide transitional specialised care,

integrated case management, disease monitoring and home-based rehabilitation and to support post-acute care as well as to incorporate acute care to the rehabilitative level.[63]

An NLC is a clinical practice of healthcare provision that includes a nurse, a patient and their family[41] involving collaboration within the multidisciplinary team (MDT), including doctors, dieticians, social workers and allied health.[63] The composition of the MDT team depends on the individual case and condition of the patient. They are operated by specialised nurses for patients' support and generally focus on the management of a specific chronic disease.[41] Nurses, as primary caregivers, deliver care with respect to patients' values, needs and preferences as well as to the patients' disease experiences and knowledge; and encourage patients in their self-management and compliance to the therapeutic regimen. They are specially trained and equipped to provide patient-centred care, providing education, and coordination of care, in regards to health promotion, prevention, and maintenance of the disease.[58]

The main components of nurse-led care include evaluation of healthcare needs, counselling, education, empowerment, treatment and case management. Care provided in NLCs enhances communication between patients and health professionals, taking into consideration individual values and disease progression Nurses relate not only to patients' symptoms but also to their psychosocial and cognitive background.[58] Thus, NLCs use a holistic approach in attending to the needs, values and preferences of patients and families based on comprehensive guidelines that apply to more than the primary condition alone.[63]

Nurse-led clinics can potentially improve treatment compliance and risk factor control and thereby provide effective secondary prevention in patients with CHD.[58] Effective secondary prevention of CHD can lead to improved health, for example, reductions in the frequency of angina and myocardial infarction and even cardiac-related death.[58] Randomised controlled trials of NLCs for CHD patients compared to usual care have not resulted in harmful effects but rather have demonstrated a positive influence on the quality of life and wellbeing in general.[58] The regular assessments of risk factors and counselling on lifestyle and health status provided within NLCs, may constructively modify such important behaviours.

3.2 Existing Systematic Review of NLCs for Coronary Heart Disease Patients

Several reviews of NLCs on cardiovascular diseases have been published in recent years. A systematic review published on this topic in 2010 by Schadewaldt and Schultz[2] concluded that NLCs were equivalent to non-nurse-led clinics, and there was no risk of poorer outcomes in NLCs. A later study and meta-analysis by Al-Mallah et al.[66] suggested that NLCs reduce major adverse cardiac events and all-cause mortality for cardiovascular patients, including angina and myocardial infarction, when compared to usual care. It appraised the effectiveness of NLCs in terms of mortality (which had not been previously included[2]) and morbidity, lipid control and adherence to medications from trials up to 2013. In addition to Al-Mallah's review, the present review included telehealth care as an intervention.

Another review by Snaterse et al.[57] summarised the effective components of nurse-coordinated clinics for the prevention of recurring cardiac events and included trials from 1990 to January 2015. It demonstrated a positive effect of NLCs versus usual care on the outcomes such as blood pressure, control of cholesterol and cessation of smoking. It included clinics with cardiac rehabilitation (CR) programs as an intervention. This is excluded in the present study as the concept of CR considerably differs from the one about NLCs with further information provided in the inclusion criteria.

A systematic review conducted in 2020 by Corones-Watkins et al.[76] aimed at synthesising evidence on the effectiveness of NLCs on patient and service outcomes after percutaneous coronary intervention (PCI), such as quality of life, medication adherence, CR attendance and psychological symptoms. It highlighted a significant gap in the research examining the effectiveness of NLCs on outcomes for patients and health services and recommended more rigorous research with an adequately powered sample size and well-defined PICO to determine the efficiency of NLCs' support.

Since the publication of the four most relevant reviews,[2,57,66,76] there has been a considerable number of relevant studies published on NLCs for patients with CHD with a focus on risk factors, health behaviours, self-management, quality of life, including depression and anxiety. An update is therefore warranted.

Therefore, the aim of the proposed study is to update the existing review of NLCs for CHD by Schadewaldt and Schultz.[2] The updated study will identify and appraise the best existing evidence on the effectiveness of NLCs and their components for patients with CHD and will present results across short- (0 to 6 months), medium- (7 to 11 months) and long-term (12 months and over) follow-up time periods. This is important to clinicians and decision-makers as well as for future clinical guidelines. The new data and new evidence may have a crucial impact on the findings of the review. In particular, the inclusion of studies in which telehealth was part of NLCs will be a significant addition to previous reviews. Furthermore, updating the existing review allows one to revise the eligibility criteria used in the review.

3.3 Review Question(s)

The research question of this review is:

What is the effectiveness of nurse-led clinics for patients with coronary heart disease on mortality and morbidity and other patient outcomes?

3.4 Inclusion Criteria

3.4.1 Population

Included in the research were studies of patients 18 years old and above with existing or newly diagnosed CHD such as angina pectoris symptoms and myocardial infarctions. Studies of heart failure, cardiomyopathies, congenital heart diseases, arrhythmias, and other cardiovascular diseases such as stroke or peripheral vascular diseases were excluded. Studies in which patients with multiple diseases were enrolled have been included when the outcomes for CHD patients were reported separately or CHD patients comprised at least 60% of the trial participants.

3.4.2 Intervention

The intervention is NLCs for patients with CHD. Nurse-led clinics are defined as a health care service that is staffed and coordinated primarily by registered nurses, advanced practice nurses and/or nurse practitioners. They deliver education, assessment, treatment and monitoring, consultation and referral to other health disciplines while collaborating with and potentially under the supervision of, doctors and other healthcare professionals.

3.4.3 Comparator

Non-nurse-led interventions included those managed by medical practitioners such as general practitioners (GPs) or specialists and any other non-nursing healthcare professional.

3.4.4 Outcomes

The outcomes that were considered in this review were:

• All-cause mortality.

• Exacerbations of heart disease symptoms or angina attacks requiring medical treatment (e.g., presentations to emergency department, readmission to hospital).

• Cardiac risk factors (e.g., smoking cessation, exercise behaviour, diet).

• Self-management (e.g., patients' ability to perform new health care behaviour and compliance (treatment adherence according to clinical guidance).

• Health status and health-related quality of life (e.g. as measured by the Seattle Angina Questionnaire, Short Form Health Survey (SF-36) or Quality of Life Index – Cardiac Version III)[68], as well as mental health outcomes including depression and anxiety, which may be measured using the SF-36, Depression Anxiety Stress Scale (DASS 21), Beck Depression and Anxiety Inventories, Hospital Anxiety and Depression Scale (HADS) and other validated tools.[69]

• Patient satisfaction (as measured using valid tools, including the 'Treatment Satisfaction' domain of the Seattle Angina Questionnaire).[68]

• Utilisation (e.g., number of consultations, length of consultation, prescriptions, tests and investigations, use of other services).

The outcomes were subdivided into short- (0-6 months), medium- (7-11) and long-term (12 months or longer) follow-up periods, as the studies included interventions with various follow-up durations .

3.5 Types of Studies

Randomised controlled trials (RCTs), including both cluster-randomised trials and individually-randomised trials, were included in this review of NLCs for CHD patients.

3.6 Methods

This review is an update of the existing review published in 2010 (Schadewaldt & Schultz),[2] which was conducted according to JBI methods. This updated SR has been undertaken in accordance with the JBI methodology for SRs of evidence synthesis[4].

3.7 Search Strategy

The search strategy aimed to identify both published and unpublished trials. A preliminary basic search of PubMed and CINAHL was carried out to locate articles on the topic, followed by analysing the titles and abstracts of the relevant studies. The reference list of all articles selected for critical appraisal was scanned for additional studies. Databases of published literature have been searched for the period January 2008 to February 2022, as the existing review covered the search to March 2008. A full search strategy for PubMed is presented in Appendix A.

3.8 Information Sources

The following bibliographic databases were used to identify trials through systematic searches:

- Cochrane Central Register of Controlled Trials (CENTRAL) on the Cochrane Library.
- PubMed.
- EMBASE (Ovid).
- PsycINFO (Ovid).
- Conference Proceedings Citation Index-S (CPCI-S) on Web of Science (Thomson Reuters).
- CINAHL (EBSCO).

• LILACS (Bireme).

The preliminary search strategy for PubMed was adapted for use in the other databases.

3.9 Study Screening and Selection

Following the search, all identified citations were collated and uploaded into EndNote X9, and duplicates were removed. At least two authors independently screened titles and abstracts of all search results against the inclusion criteria. The first author screened all the search results, and each of the three supervisors screened one-third of the articles. A third author was involved in reaching a consensus decision regarding any disagreements that arose between the reviewers on inclusion. The full text of publications that met the inclusion criteria was retrieved, and the citations were imported into JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI).[70] Ineligible studies that did not meet the criteria were excluded, and the reasons are provided in Appendix B.

3.10 Critical Appraisal

Two independent reviewers critically appraised the methodological quality of the selected study by applying standard critical appraisal instruments from JBI.[72] Where disagreements emerged during the assessment process, they were resolved through consultation or deploying a third reviewer. The results are presented both in a table and in narrative form. The authors undertook data extraction and synthesis of all studies, regardless of the results of their methodological quality.

3.11 Data Extraction

The primary reviewer extracted outcome data from included studies and transferred data into the Review Manager software.[73] The following study characteristics were included.

1. Methods: study design, total duration of study, number of study centres and location, the study setting, withdrawals, and date of the study.

2. Participants: number, mean age ± SD, age range, gender, the severity of the condition, diagnostic criteria, existing heart disease, inclusion criteria, and exclusion criteria.

3. Interventions: intervention, comparison.

4. Outcomes: primary and secondary outcomes specified and collected, and time points reported.

5. Results. Data were entered manually into RevMan and visually compared to the original trial reports to ascertain the correct data entry. A second review author spot-checked study characteristics for accuracy against the trial report.

When necessary, investigators of original studies were contacted in order to verify key study characteristics or obtain missing outcome data.

3.12 Data Synthesis

Data synthesis was performed using Review Manager.[73] Dichotomous data were analysed as odds ratios with 95% confidence intervals CI), and continuous data as mean differences or standardised mean differences with 95% confidence intervals. Data are presented as a scale with a consistent direction of effect.

The I^2 statistic was used to measure heterogeneity among the trials in each analysis. With moderate to significant heterogeneity in most of the meta-analysis results, random-effects models were used, which deliver a more conservative test by producing wider confidence intervals for the overall effect size.[70] A narrative synthesis was used to describe results in events where only one study was included, and statistical pooling was not possible.

Results of the studies included in the 2010 review are reported in this updated review when they could be used in the meta-analysis. Critical appraisal and data extraction were carried out for the 2010 review studies.

3.13 Assessing Certainty in the Findings

The quality of evidence was assessed according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework by creating a 'Summary of findings' table for the primary outcomes using the GRADEPro tool.[34] This table is used to summarise evidence from a SR to be used when making recommendations for practice. It contains main information about outcomes, statistical results and quality of evidence grading. The certainty of the evidence was assessed as either high, moderate, low or very low for each outcome. This was achieved by using the five GRADE criteria for upgrading or

downgrading the certainty of the evidence (risk of bias, consistency of effect, imprecision, indirectness, and publication bias). The main reasons for upgrading or downgrading the certainty of the evidence were recorded in the footnotes of the 'Summary of findings'. The findings for each intervention were summarised, and the certainty of the evidence was graded for each of the outcomes in the 'Summary of findings' tables.

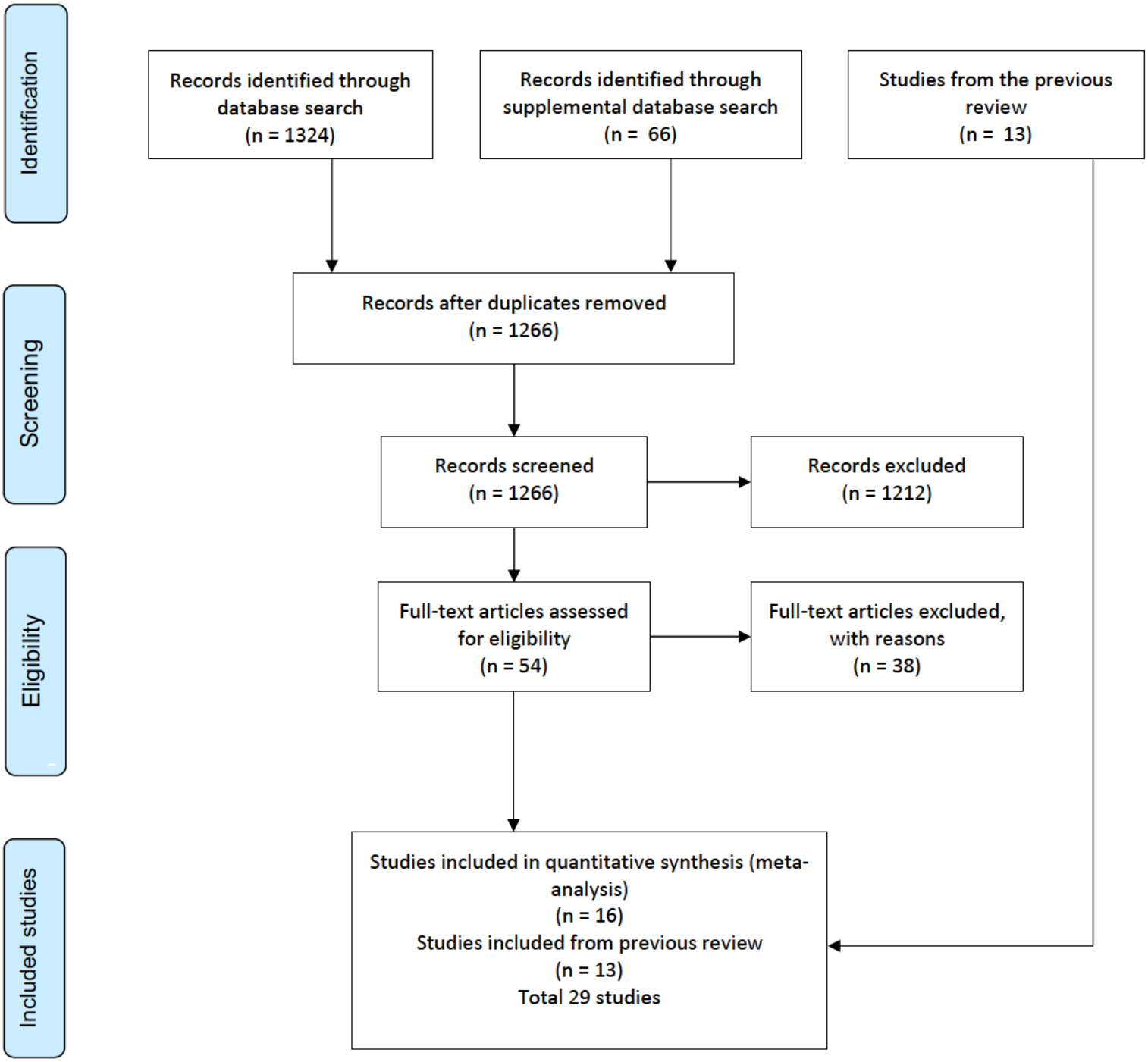
3.14 Results

3.14.1 Study selection

Our initial search from 2008 to 2018 identified a total of 1324 titles, from which 124 duplicates were removed (Figure 1). A supplemental search of publications from 2018 up to February 2022 yielded 66 more articles. A large number of trials identified through the initial database search had to be excluded, as the population included participants with cardiovascular diseases other than CHD, like heart failure, congenital heart disease, cardiac arrhythmias or stroke. After examining all of the titles and abstracts against inclusion criteria, the full text of 54 potentially relevant publications were sourced.

After a full-text examination against inclusion criteria, 38 publications were eliminated, and an appraisal was conducted on 16 articles. As shown in Figure 1, all 16 publications identified in the search from 2008 to 2022 were included in the review, in addition to 13 studies published prior to 2008 and included in the 2010 review. Authors of three of the 16 studies[7,10,11] were contacted by email with the request to provide missing data for meta-analysis. Since the authors could not be contacted or did not respond to email, we were unable to include those studies for inclusion in this review. The list of the publications with missing data is presented in the second table in Appendix B.

Figure 1 PRISMA Flow Diagram



3.14.2 Characteristics of included articles

There are 16 studies[5 20] included in this review comprising the period of 2008 to 2022 and 13 studies[21 33] from the previous review from 2002 to 2008. Across all 29 studies, 17 studies were conducted in Europe,[5,8 11,15,18,20,25 33] five in Australia,[6,7,17,22,23] three in China,[16,19,24] one in South Korea,[12] two in Canada,[14,21] and one in Brazil.[13] All studies are randomised-controlled trials with sample sizes from 33 to 3715.

Five studies evaluated all-cause mortality,[8,21,27,33,77] two trials investigated chest pain exacerbations, including those requiring medical treatment [5,31], 12 trials[6,8,21,22,24 26,30,78 81] measured changes in risk factors for cardiac patients, eight trials[6,8,14,17,78 81] provided data on self-management of health behaviour, six studies[6,8,21,27,30,80] investigated patients' compliance to the treatment and ten trials[5,6,8,10,11,14,17,20,78,79] provided self-reported measurements of quality of life for cardiac patients. Less frequently considered outcomes were utilization of services,[6,8] no publications were on patient satisfaction; thus, the meta-analysis was not possible for these outcomes.

The educational level of nursing personnel staffing the NLCs in the included studies varied. Although all were registered nurses with at least a bachelor's degree, some had experience in cardiovascular care and additional training in motivational counselling and therapies used during interventions. The follow-up period also varied significantly between studies: eight studies had 12 months and over follow-up, while eight had short- and medium-term follow-up of 3 to 6 and 7 to 12 months, respectively.

The intensity and format of the interventions varied from developing a personal health plan, face-to-face visits and telephone conversations to tailored education, interpersonal counselling and coaching on behavioural modification strategies. Table 3 in Appendix C provides an overview of the characteristics of included studies, including population, interventions, setting, and outcomes.

3.14.3 The methodological quality of included studies and heterogeneity

The studies included in the present review had overall moderate methodological quality and risk of bias (Figure 2, Figure 3). The JBI critical appraisal tool for RCTs, used to assess the

quality of studies, showed that the included studies met a mean of 8 appraisal tool criteria out of 13, ranging from 5 to 11 (see table 1 in Appendix D). Most studies had certain methodological limitations relating to blinding of personnel and participants, attrition bias, allocation concealment, delivering treatment, and research contamination, which occasionally resulted in the downgrading of the evidence. Though lack of blinding is a serious limitation, blinding can be challenging in some trials and not achievable for structural interventions, such as NLCs.

The potential risk of publication bias was not assessed due to the limited number of studies included in analysing each reported outcome.

Figure 2 Risk of Bias Graph

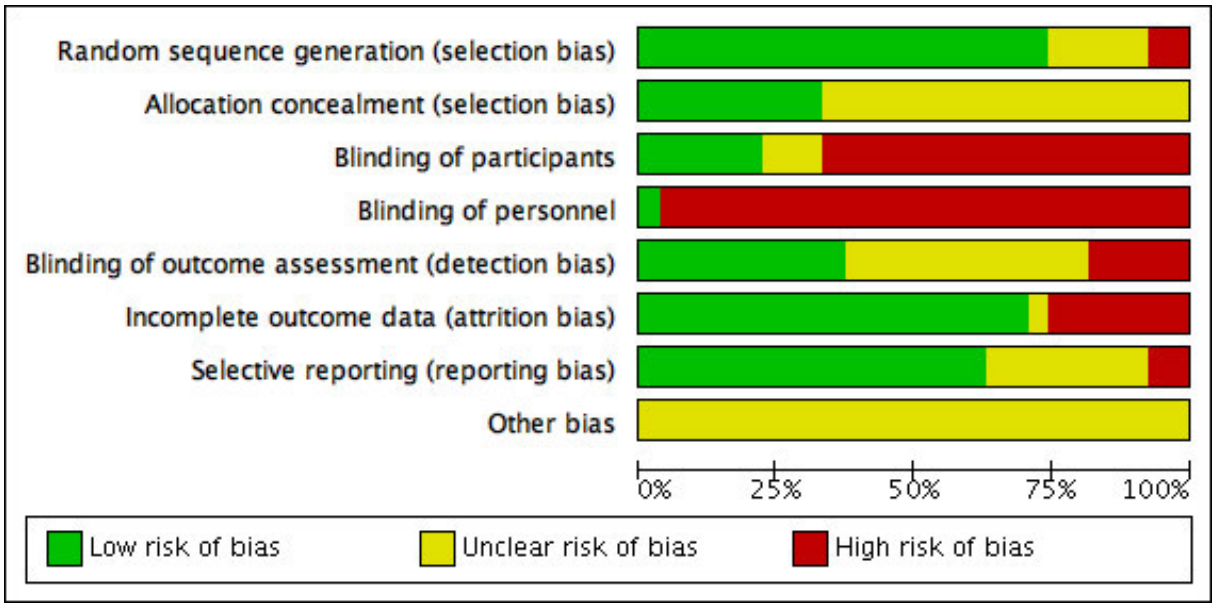
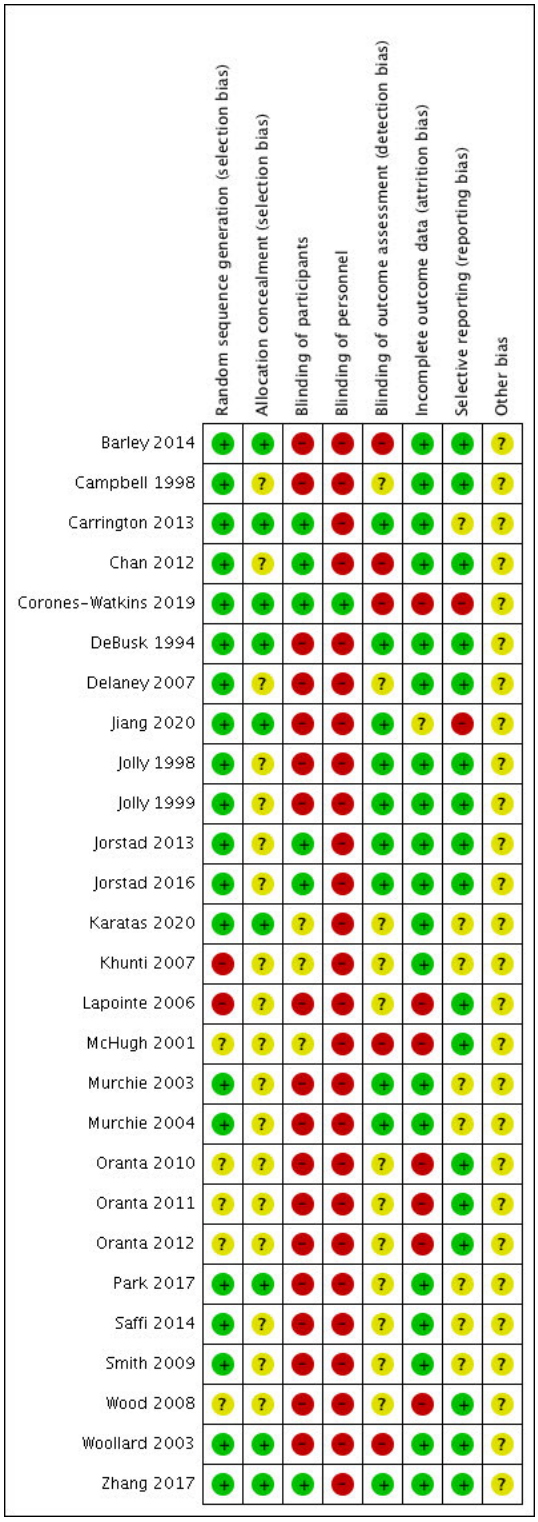


Figure 3 Risk of Bias Summary



There was little to no heterogeneity in the analysis of exacerbation of all-cause mortality, chest pain and some health behaviours. However, other outcomes (cardiac risk factors, health behaviours) demonstrated moderate to substantial statistical heterogeneity, signifying

inconsistency in the results of included studies. The causes for statistical heterogeneity could be differences in the intensity of interventions, diverse expertise and training of nurses, diversity and complexity of patients, as well as variations in health care providers, policies and procedures on NLCs in different countries.

3.14.4 Summary of findings

SOF 1 Nurse-led clinics compared to usual care in reducing all-cause mortality

Certainty assessment							№ o patients		E ect		Certainty	mportance
№ o studies	Study design	Risk o bias	nconsistency	ndirectness	mprecision	Other considerations	nurse-led clinics	usual care	Relative (95% C)	Absolute (95% C)		
All-cause mortality												
5	randomised trials	not serious	not serious[a]	not serious	serious[b]	none	54/1651 (3 3%)	72/1677 (4 3%)	**OR 0.78** (0 54 to 1 13)	**9 fewer per 1,000** (rom 19 ewer to 5 more)	⨁⨁⨁◯ Moderate	CR CAL

CI: confidence interval **OR:** odds ratio
a No observed heterogeneity
b Small sample size a small number of events less than 300 (42 in intervention 62 in comparison) Confidence intervals do include null effect

SOF 2 Nurse-led clinics compared to usual care in reducing exacerbations of chest pain requiring medical treatment

Certainty assessment							№ o patients		E ect		Certainty	mportance
№ o studies	Study design	Risk o bias	nconsistency	ndirectness	mprecision	Other considerations	nurse-led clinics	usual care	Relative (95% C)	Absolute (95% C)		
Chest pain long-term												
2	randomised trials	not serious [a]	not serious [b]	not serious	serious [c]	none	254/540 (47 0%)	280/535 (52 3%)	**OR 0.81** (0 64 to 1 04)	**53 fewer per 1,000** (rom 111 ewer to 10 more)	⨁⨁⨁◯ MODERA E	CR CAL

CI: Confidence interval **OR:** Odds ratio
a Most information is from studies at low or unclear risk of bias
b P-value is 0 40 results of the test are not statistically significant the minimal overlap of confidence intervals
c Small sample size a small number of events less than 300 (254 in intervention 280 in comparison) Confidence intervals do include null effect

SOF 3 Nurse-led clinics compared to usual care in reducing physical cardiac risk factors

Certainty assessment							№ o patients		E ect		Certainty	mportance
№ o studies	Study design	Risk o bias	nconsistency	ndirectness	mprecision	Other considerations	nurse-led clinics	usual care	Relative (95% C)	Absolute (95% C)		
Systolic BP continuous med-term												
3	randomised trials	not serious[a]	serious[b]	not serious	not serious[c]	none	185	181	-	MD **10.96 lower** (15 49 lower to 6 43 lower)	⨁⨁⨁◯ Moderate	CR CAL
Diastolic BP continuous med-term												
3	randomised trials	not serious	serious[d]	not serious	serious[e]	none	185	181	-	MD **8.47 lower** (13 83 lower to 3 12 lower)	⨁⨁◯◯ Low	CR CAL
Systolic BP dichotomous long-term												
3	randomised trials	not serious[a]	serious[f]	not serious	not serious[g]	none	1086/1558 (69 7%)	961/1600 (60 1%)	**OR 1.50** (1 17 to 1 92)	**92 more per 1,000** (rom 37 more to 142 more)	⨁⨁⨁◯ Moderate	CR CAL
Diastolic BP dichotomous long-term												
3	randomised trials	not serious	not serious	not serious	not serious	none	1380/1558 (88 6%)	1340/1600 (83 8%)	**OR 1.50** (1 19 to 1 88)	**48 more per 1,000** (rom 22 more to 69 more)	⨁⨁⨁⨁ High	CR CAL
Systolic BP continuous long-term												
2	randomised trials	serious[h]	not serious[i]	not serious	serious[j]	none	86	81	-	MD **9.06 lower** (16 59 lower to 1 52 lower)	⨁⨁◯◯ Low	CR CAL
Diastolic BP continuous long-term												
2	randomised trials	serious[h]	serious[k]	not serious	serious[j]	none	86	81	-	MD **8.09 lower** (17 99 lower to 1 81 higher)	⨁◯◯◯ Very low	CR CAL

Total cholesterol long-term dichotomous												
4	randomised trials	not serious	serious[l]	not serious	not serious	none	1242/2066 (60 1%)	1067/2067 (51 6%)	**OR 0.69** (0 46 to 1 05)	**92 fewer per 1,000** (rom 187 ewer to 12 more)	⊕⊕⊕◯ Moderate	CR CAL
Total cholesterol medium-term continuous												
2	randomised trials	not serious	serious[m]	not serious	serious[n]	none	130	131	-	SMD **0.46 lower** (1 13 lower to 0 21 higher)	⊕⊕◯◯ Low	CR CAL
Total cholesterol long-term continuous												
2	randomised trials	serious[o]	serious[p]	not serious	serious[n]	none	86	83	-	SMD **0.47 lower** (1 49 lower to 0 54 higher)	⊕◯◯◯ Very low	CR CAL
HDL change from baseline to 12 months												
3	randomised trials	not serious[q]	serious[r]	not serious	serious[s]	none	424	415	-	SMD **0.1 higher** (0 24 lower to 0 44 higher)	⊕⊕◯◯ Low	CR CAL
HDL change from baseline to 18 months												
2	randomised trials	serious[a]	not serious	not serious	serious[j]	none	64	63	-	SMD **0.08 lower** (0 43 lower to 0 27 higher)	⊕⊕◯◯ Low	CR CAL
HDL short-term continuous												
2	randomised trials	not serious	serious[t]	not serious	serious[j]	none	132	131	-	SMD **0.16 lower** (0 57 lower to 0 24 higher)	⊕⊕◯◯ Low	CR CAL

CI: confidence interval **MD:** mean difference **OR:** odds ratio **SMD:** standardised mean difference
a Most information is from studies at low or unclear risk of bias
b 2 is 52% moderate heterogeneity
c Small sample size but confidence intervals do not include null effect and are all on one side of the decision threshold showing appreciable benefit do not downgrade
d 2 is 82% considerable heterogeneity
e Small sample size less than 300 (185 - intervention 181 - control group) does not meet O S threshold
f 2 is 58% moderate heterogeneity total variability among effect sizes is caused by true heterogeneity between studies
g Large sample size a large number of events over than 300 (1086 in intervention 961 in comparison) Confidence intervals do not include null effect
h Most information is from studies at high or unclear risk of bias downgrade by one level
i Substantial heterogeneity of 61% point estimates relatively far and C does not overlap downgrade by one level
j Small sample size does not meet O S threshold
k Considerable heterogeneity of 91% Confidence intervals do include null effect and appreciable benefit downgrade
l Substantial heterogeneity of 88% point estimates are relatively far and C do not overlap
m Substantial heterogeneity of 82% point estimates are far and C do not overlap
n O S is not met
o Most information is from studies at high or unclear risk of bias
p Considerable heterogeneity of 91% Confidence intervals do include null effect and appreciable benefit
q Jorstad 2013 has 54% weight do not downgrade
r 2 is 58% moderate heterogeneity total variability among effect sizes is caused by true heterogeneity between studies
s Wide confidence intervals Optimal information size is not met
t Moderate heterogeneity of 53%

SOF 4 Nurse-led clinics compared to usual care in improving health behaviour

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ o studies	Study design	Risk o bias	nconsistency	ndirectness	mprecision	Other considerations	nurse-led clinics	usual care	Relative (95% C)	Absolute (95% C)		
Smoking long-term												
5	randomised trials	not serious	serious [e]	not serious	serious [f]	none	941/1238 (76 0%)	962/1348 (71 4%)	**OR 0.77** (0 50 to 1 19)	**56 fewer per 1,000** (rom 159 ewer to 34 more)	⊕⊕◯◯ LOW	MPOR AN
Fasting blood sugar medium term												
2	randomised trials	not serious	not serious	not serious	serious [g]	none	130	131	-	SMD **0.39 lower** (0 63 lower to 0 14 lower)	⊕⊕⊕◯ MODERA E	MPOR AN
BMI long-term continuous												
2	randomised trials	serious [c]	not serious	not serious	serious [b]	none	87	85	-	MD **1 lower** (2 05 lower to 0 05 higher)	⊕⊕◯◯ LOW	MPOR AN
BMI long-term dichotomous												
2	randomised trials	not serious	serious [h]	not serious	serious [i]	none	334/1304 (25 6%)	299/1338 (22 3%)	**OR 0.96** (0 50 to 1 83)	**7 fewer per 1,000** (rom 98 ewer to 121 more)	⊕⊕◯◯ LOW	MPOR AN

Weight long-term												
2	randomised trials	not serious	not serious	not serious	serious [j]	none	295	298	-	MD **1.16 lower** (3 77 lower to 1 45 higher)	⊕⊕⊕◯ MODERA E	MPOR AN
Ideal waist circumference long-term												
3	randomised trials	not serious	serious [k]	not serious	serious [i]	none	535/1561 (34 3%)	477/1601 (29 8%)	**OR 0.93** (0 57 to 1 52)	**15 fewer per 1,000** (rom 103 ewer to 94 more)	⊕⊕◯◯ LOW	MPOR AN
Physical activity (>30 min > 4x a week)												
3	randomised trials	not serious	serious [l]	not serious	not serious [m]	none	993/1888 (52 6%)	563/1908 (29 5%)	**OR 0.43** (0 20 to 0 93)	**143 fewer per 1,000** (rom 218 ewer to 15 ewer)	⊕⊕⊕◯ MODERA E	MPOR AN

CI: Confidence interval **OR:** Odds ratio **SMD:** Standardised mean difference **MD:** Mean difference
a 2 is 58% moderate heterogeneity total variability among effect sizes is caused by true heterogeneity between studies
b Small sample size does not meet O S threshold
c Most information is from studies at low or unclear risk of bias
d Substantial heterogeneity of 71% point estimates are far and C do not overlap
e Substantial heterogeneity of 77% point estimates relatively far and C does not overlap
f Wide confidence intervals uncertainty about magnitude of effect
g Small sample size but confidence intervals do not include null effect and are all on one side of the decision threshold showing appreciable benefit
h Considerable heterogeneity of 90% Confidence intervals do not overlap
i O S is met but confidence intervals do include null effect and appreciable benefit
j Confidence intervals do include null effect and appreciable benefit
k Considerable 2 (87%) point estimates relatively far and C do not overlap
l Considerable [2] (97%)
m O S is met confidence intervals do not include null effect and are all on one side of the decision threshold showing appreciable benefit

SOF 5 Nurse-led clinics compared to usual care in improving self-management (e.g. patients' ability to perform new health care behaviour and compliance (treatment adherence according to clinical guidance))

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	nurse-led clinics	usual care	Relative (95% CI)	Absolute (95% CI)		
ACE Inhibitors long-term												
3	randomised trials	not serious	serious[a]	not serious	serious[b]	none	868/1557 (55.7%)	893/1601 (55.8%)	**OR 0.92** (0.64 to 1.34)	**21 fewer per 1,000** (from 111 fewer to 70 more)	⊕⊕◯◯ Low	IMPORTANT
Antiplatelet long-term												
4	randomised trials	not serious	serious[c]	not serious	not serious	none	1902/2132 (89.2%)	1840/2163 (85.1%)	**OR 1.31** (0.83 to 2.07)	**31 more per 1,000** (from 25 fewer to 71 more)	⊕⊕⊕◯ Moderate	IMPORTANT

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	nurse-led clinics	usual care	Relative (95% CI)	Absolute (95% CI)		
Beta-blockers long-term												
3	randomised trials	not serious	serious[d]	not serious	serious[b]	none	1125/1557 (72.3%)	1174/1601 (73.3%)	**OR 0.99** (0.67 to 1.45)	**2 fewer per 1,000** (from 85 fewer to 66 more)	⨁⨁◯◯ Low	IMPORTANT
Statins long-term												
6	randomised trials	not serious	serious[e]	not serious	serious[f]	none	1860/2800 (66.4%)	1633/2817 (58.0%)	**OR 1.33** (0.82 to 2.15)	**67 more per 1,000** (from 49 fewer to 168 more)	⨁⨁◯◯ Low	IMPORTANT
Diuretics long-term												
2	randomised trials	not serious	serious[g]	not serious	serious[h]	none	134/612 (21.9%)	113/610 (18.5%)	**OR 0.81** (0.61 to 1.07)	**30 fewer per 1,000** (from 63 fewer to 10 more)	⨁⨁◯◯ Low	IMPORTANT

CI: confidence interval; **OR:** odds ratio
a. Widely differing estimates of treatment effect, wide variance of point estimates, substantial heterogeneity of 81%
b. Confidence intervals do include null effect, and appreciable benefit.
c. Substantial heterogeneity of 78%, wide variance of point estimates
d. Substantial heterogeneity of 79%, widely differing estimates of treatment effect
e. Considerable heterogeneity of 91%, wide variance of point estimates
f. Confidence intervals do include null effect, and appreciable benefit.
g. Moderate heterogeneity of 56%, widely differing estimates of treatment effect
h. OIS is not met, small sample size, small number of events

SOF 6 Health status and health-related quality of life

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ o studies	Study design	Risk o bias	nconsistency	ndirectness	mprecision	Other considerations	nurse-led clinics	usual care	Relative 95% C)	Absolute (95% C)		
QOL physical short-term												
2	randomised trials	not serious	serious [a]	not serious	serious [b]	none	73	72	-	MD **0.58 higher** (1 82 lower to 2 98 higher)	⨁⨁◯◯ LOW	MPOR AN
QOL physical medium term												
3	randomised trials	not serious	serious [c]	not serious	serious [b]	none	166	170	-	SMD **0.26 higher** (0 to 0 52 higher)	⨁⨁◯◯ LOW	MPOR AN

QOL physical long-term												
5	randomised trials	serious [d]	serious [e]	not serious	serious [b]	none	966	966	-	SMD **0.22 higher** (0 03 higher to 0 4 higher)	⊕◯◯◯ VERY LOW	MPOR AN
QOL mental short-term												
3	randomised trials	serious [d]	serious [e]	not serious	not serious	none	654	635	-	MD **6.79 higher** (0 04 higher to 13 54 higher)	⊕⊕◯◯ LOW	MPOR AN
QOL mental medium-term												
3	randomised trials	not serious	serious [c]	not serious	serious [b]	none	168	171	-	MD **3.51 higher** (2 28 lower to 9 3 higher)	⊕⊕◯◯ LOW	MPOR AN

QOL mental long-term												
5	randomised trials	serious [d]	serious [c]	not serious	not serious	none	983	958	-	MD **3.14 higher** (0 49 lower to 6 77 higher)	⊕⊕◯◯ LOW	MPOR AN
Social functioning long-term												
3	randomised trials	not serious	serious [c]	not serious	serious [b]	none	697	675	-	MD **5.1 higher** (2 35 lower to 12 56 higher)	⊕⊕◯◯ LOW	MPOR AN
Physical component summary med-term												
3	randomised trials	not serious	serious [a]	not serious	serious [c]	none	209	205	-	MD **2.56 higher** (0 06 lower to 4 52 higher)	⊕⊕◯◯ LOW	MPOR AN
Mental component summary med-term												
2	randomised trials	not serious	serious [a]	not serious	serious [c]	none	168	165	-	MD **3.32 higher** (7 64 lower to 14 28 higher)	⊕⊕◯◯ LOW	MPOR AN
Depression and anxiety												
3	randomised trials	not serious	serious [c]	not serious	not serious	none	870	863	-	SMD **0.47 higher** (0 48 lower to 1 41 higher)	⊕⊕⊕◯ MODERA E	MPOR AN

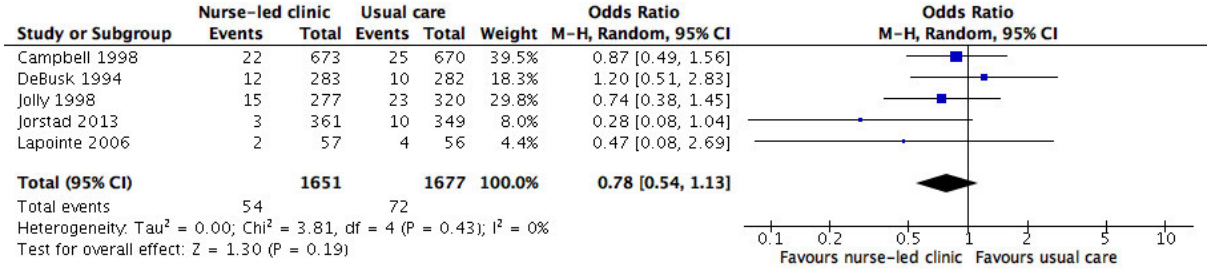
Depression and anxiety												
5	randomised trials	not serious	serious [f]	not serious	not serious	none	100/1153 (8 7%)	83/1173 (7 1%)	**OR 1.27** (0 93 to 1 72)	**17 more per 1,000** (rom 5 ewer to 45 more)	⊕⊕⊕◯ MODERA E	MPOR AN

CI: Confidence interval **MD:** Mean difference **SMD:** Standardised mean difference **OR:** Odds ratio
a Widely differing estimates of treatment effect
b Small sample size small number of events wide confidence intervals
c Widely differing estimates of treatment effect no overlap of confidence intervals substantial heterogeneity
d Most information is from studies at high or unclear risk of bias
e No overlap of confidence intervals substantial heterogeneity
f Widely differing estimates of treatment effect no overlap of confidence intervals

3.14.5 All-cause mortality

Five studies evaluated mortality.[8,21,27,33,77] *The previous SR evaluated the outcomes of mortality, however, the data was insufficient in power to draw final conclusions for the effectiveness of nurse-led clinics and therefore they were not reported in the final outcomes.* Based on the meta-analysis, NLCs may slightly contribute to the reduction of all-cause mortality among cardiac patients in comparison to usual care at the 12+ months follow-up (odds ratio (OR) of 0.78; 95% CI, 0.54 to 1.13, P=0.19; 3328 participants) (Figure 4). While not statistically significant, the absolute effect on mortality showed that among those patients who attended NLCs, 9 fewer patients per 1,000 people died (from 19 fewer to 5 more) (refer to the Summary of Findings Table SOF 1). No statistical heterogeneity was observed in the analysis of all-cause mortality with I^2=0% and P=0.43. The evidence is of moderate certainty due to the small number of events and wide CIs. The Campbell trial demonstrated a sustained reduction of mortality after a 4-year follow-up (CI 0.57-1.01, P=0.06; 1343 participants) (reported in the Delaney et al. study)[29] (Table 1, Appendix E).

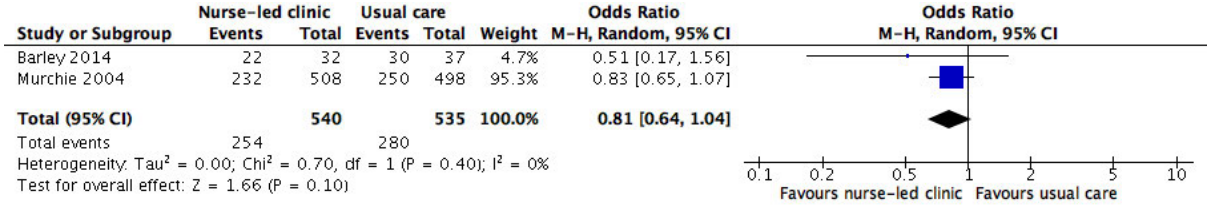
Figure 4 Effect of nurse-led clinics on all-cause mortality in the long-term



3.14.6 Exacerbations of chest pain requiring medical treatment

Two trials investigated chest pain exacerbations requiring medical treatment. [5,31] Attendance at NLCs may slightly reduce symptoms of chest pain in the long term (OR 0.81; 95% CI 0.64 to 1.04; P=0.10; 1075 participants) (Figure 5). Although not statistically significant, the absolute effect on chest pain showed that among those patients who attended NLCs, 53 fewer patients per 1,000 people experienced exacerbations (SOF 2). The evidence is of moderate certainty due to the small sample size, a small number of events and minimal overlap of CIs. No heterogeneity was observed in the analysis of chest pain with I^2=0% and P=0.40. No meta-analysis was possible for short- and medium-term measures (3-6 months) of heart disease, and data from one study[5] (Table 2, Appendix E) for these follow-up periods showed no significant reduction of chest pain symptoms.

Figure 5 Effect of nurse-led clinics on patients experiencing chest pain in the long-term



3.14.7 Cardiac risk factors

Twelve trials[6,8,21,22,24 26,30,78 81] measured changes in risk factors for cardiac patients. Risk factor outcomes varied across trials and have been grouped into two categories: blood pressure and blood lipids. Findings for each of these categories are presented below.

3.14.8 Blood pressure

Blood pressure as an outcome was reported in ten studies (five included from the 2010 review[22,24 26,30] and five studies added in this update).[6,8,79 81] The data were presented both as continuous and dichotomous outcomes revealing consistent results. Only data for medium- and long-term outcomes were available.

For systolic BP in the medium term, the mean BP was 10.96 mm Hg lower in NLCs (95% CI -15.49 to 6.43, P<0.00001, three studies, 366 participants) (Figure 6). Moderate heterogeneity of 52% was identified for systolic BP. For diastolic BP in the medium term, the mean BP was 8.47 mm Hg lower in NLCs (95% CI -13.83 to -3.12, P=0.002, three studies, 366 participants) (Figure 7). High heterogeneity of 82% may be attributed to the

heterogeneous cohort of the included population and the presence of vascular and other co-morbidities like diabetes mellitus and chronic kidney disease considerably affecting BP. Evidence is of low to moderate certainty for systolic and diastolic BP due to the high risk of bias, small sample size and inconsistency.

Figure 6 Effect of nurse-led clinics on systolic BP (mmHg) in the medium-term (continuous data)

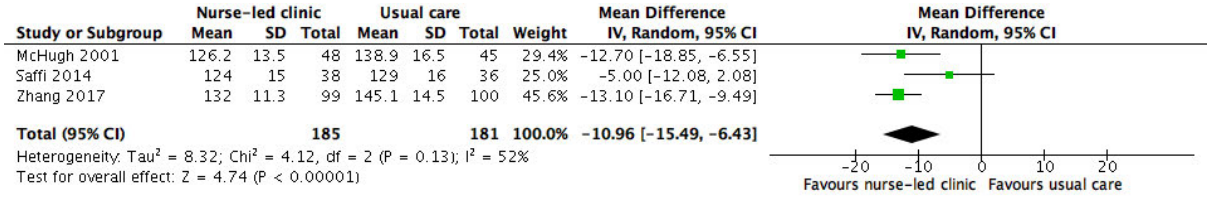
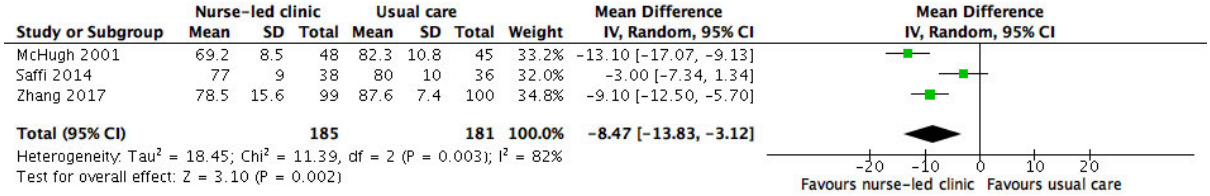


Figure 7 Effect of nurse-led clinics on diastolic BP (mmHg) in the medium-term (continuous data)



For BP as a dichotomous variable, the results from three studies in the long term were consistent with the medium-term continuous data, even though different studies assessed three different timeframes. The OR in Figure 8 and Figure 9 show statistically significant benefits from the intervention in the long-term on achieving the targeted systolic BP of <140 mm Hg (OR 1.50, 95% CI 1.17, 1.92; P=0.002; three studies with 3158 participants) and diastolic BP of <90 mm Hg (OR 1.50, 95% CI 1.19, 1.88; P=0.0006; three studies with 3158 participants). Evidence is of moderate to high certainty. Heterogeneity of 58% and 13%, respectively, was moderate to low.

Figure 8 Effect of nurse-led clinics on achieving targeted systolic BP (mmHg) in the long-term (dichotomous data)

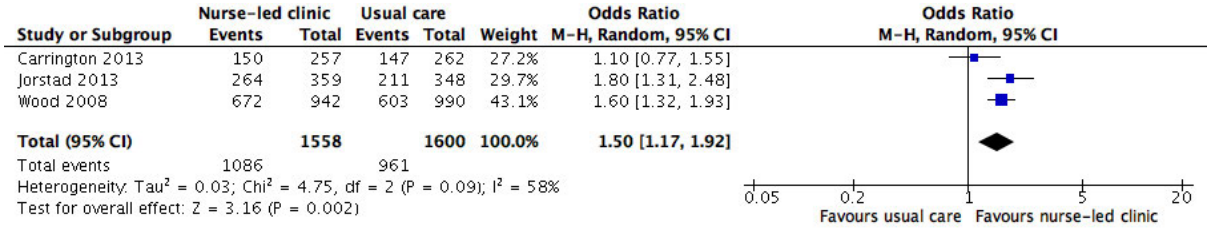
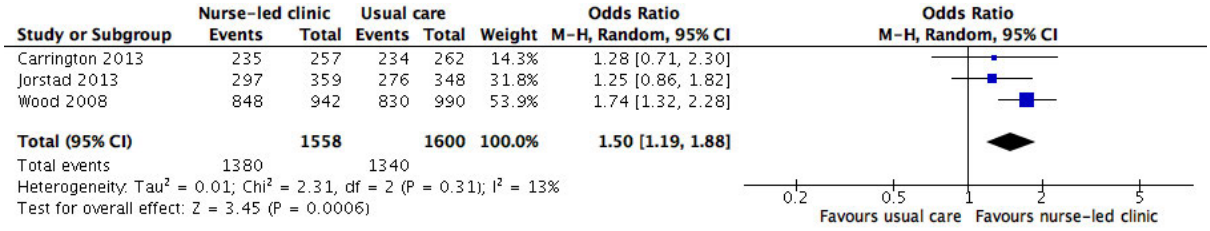


Figure 9 Effect of nurse-led clinics on achieving targeted diastolic BP (mmHg) in the long-term (dichotomous data)



For BP as a continuous variable, the results from two studies in the long-term (Figure 10 and Figure 11) were consistent with the results from three studies in the medium-term follow-up systolic BP (95% CI -16.59 to -1.52; P=0.02; two studies with 167 participants) and diastolic BP (95% CI -17.99 to 1.81; P=0.11; two studies with 167 participants). Systolic BP improved significantly in the NLC group, however, this was significant for diastolic BP.

Figure 10 Effect of nurse-led clinics on systolic BP (mmHg) in the long-term (continuous data)

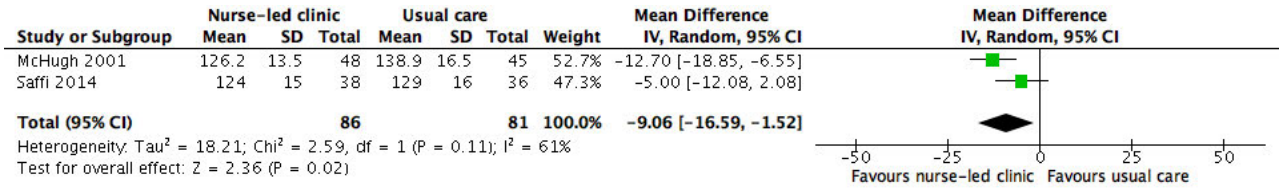
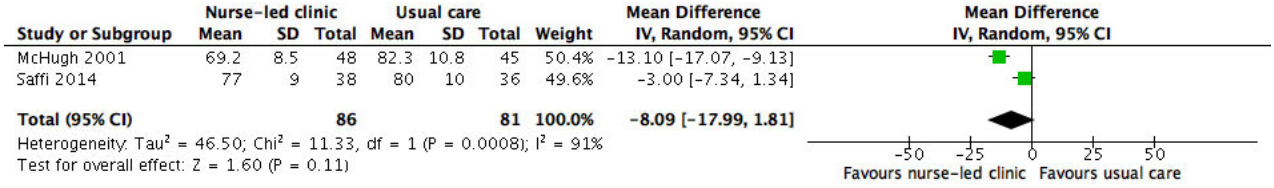


Figure 11 Effect of nurse-led clinics on diastolic BP (mmHg) in the long-term (continuous data)



The data from long-term dichotomous data was not available for meta-analysis.

3.14.9 Blood lipids

Six new studies[6,8,78 81] were added in this update to six existing studies[21,22,24,25,30,82] of NLCs' impact on blood lipids, including total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C), providing a total of 12 studies for the meta-analyses.

The results of the meta-analysis of TC as a continuous variable in four different studies in the medium- and long-term, respectively, did not identify any advantages related to NLCs when using an SMD approach. This was due to differences in units used between studies (SMD -0.46, 95% CI -1.13 to 0.21; P=0.18; 2 studies with 261 participants), (SMD -0.47, 95% CI -1.49 to 0.54; P=0.36; 2 studies with 169 participants), (Figure 12 and Figure 13). Evidence is of very low to low certainty due to the risk of bias, small sample size and serious inconsistency. Additionally, significant heterogeneity of I^2=82% and 90% was observed in the meta-analyses.

Figure 12 Effect of nurse-led clinics on total cholesterol in the medium-term (continuous data)

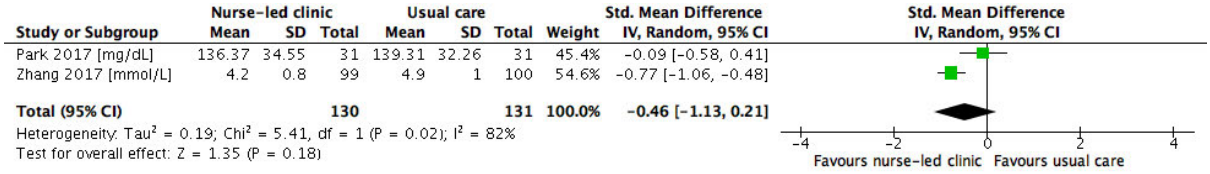
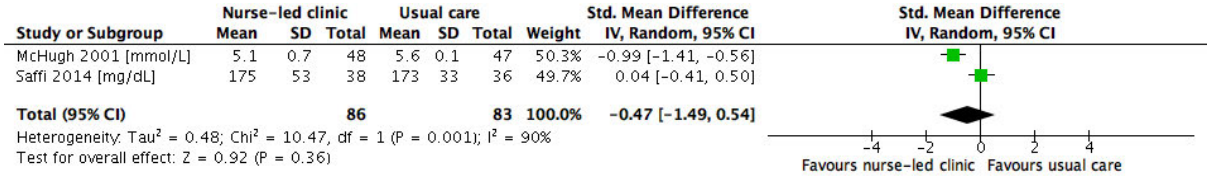


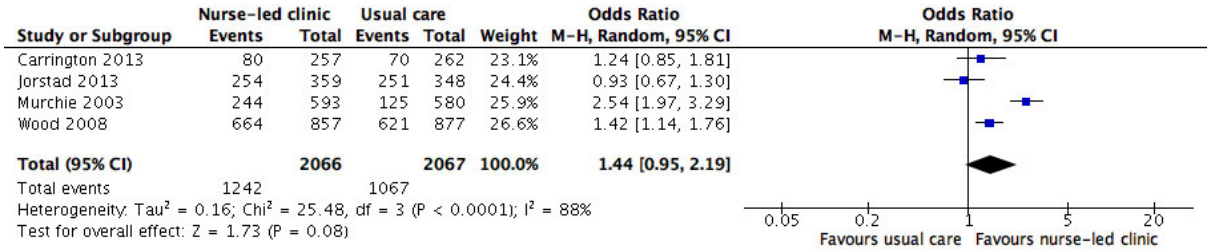
Figure 13 Effect of nurse-led clinics on total cholesterol in the long-term (continuous data)



Four studies measured the dichotomous outcomes of achieving a TC of ≤4-4.5mmol/L (Figure 14) after 12 months. There was no statistically significant difference between the two groups (OR 1.44, 95% CI 0.95 to 2.19; P=0.08; 4 studies with 4133 participants). Evidence is of a moderate certainty due to the small sample size and significant inconsistency. The significant heterogeneity of the outcomes may be attributed to the intensity of the interventions as well as the disease complexity of the patients participating in the trial.

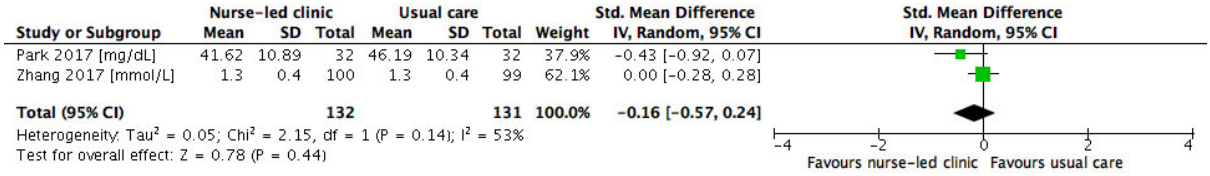
Results from the medium-term follow-up at 6 months[8] that could not be pooled in the meta-analysis were consistent with the above results (Table 3, Appendix E) 78% in NLCs versus 70% of usual care.

Figure 14 Effect of nurse-led clinics on achieving targeted total cholesterol in the long-term (dichotomous data)



HDL-C has an inverse association with the risk of cardiac diseases,[83] i.e. increasing HDL-C concentrations are associated with decreasing CHD risks. The studies included in the review (Figure 15) suggested that NLCs did not increase HDL-C compared to usual care at 6 months of follow-up (SMD=-0.16, 95% CI -0.57 to 0.24; P=0.44, 263 participants).

Figure 15 Effect of nurse-led clinics on HDL-C in the short-term (continuous data)



Results from the meta-analyses on the change of HDL-C levels (Figure 16 and Figure 17) did not identify significant differences between the groups at the 12 to 18-months follow-up (MD 0.04, 95% CI -0.0 to 0.12; P=0.35; 3 studies with 839 participants) nor the 18-month follow-up (MD -0.01, 95% CI -0.06 to 0.04; P=0.67; 2 studies with 127 participants), respectively.

Figure 16 Effect of nurse-led clinics on change of HDL-C(units) in the medium term (continuous data)

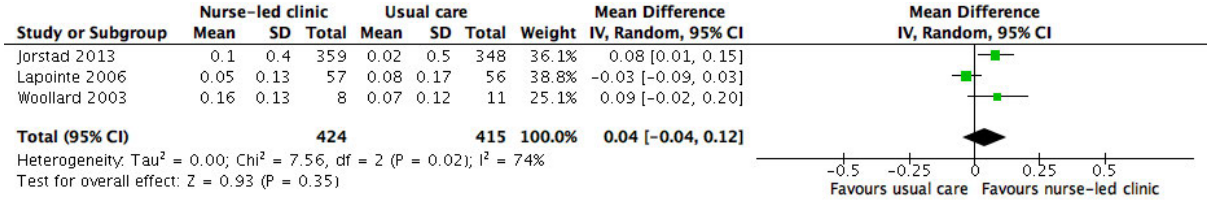


Figure 17 Effect of nurse-led clinics on change of HDL (units) in the long-term (continuous data)

Meta-analysis was not possible for triglyceride and low-density lipoprotein cholesterol (LDL), and some individual studies assessing TC and HDL with data presented in Table 3 (Appendix E). No statistically significant differences were identified for HDL, LDL and triglycerides outcomes at the mid- and long-term follow-up in individual studies. Achieving certain TC levels was more successful in patients who attended NLCs at the 6-months follow-up in one study (OR 1.53 95% CI 1.09 to 2.14; P=0.01).[8]

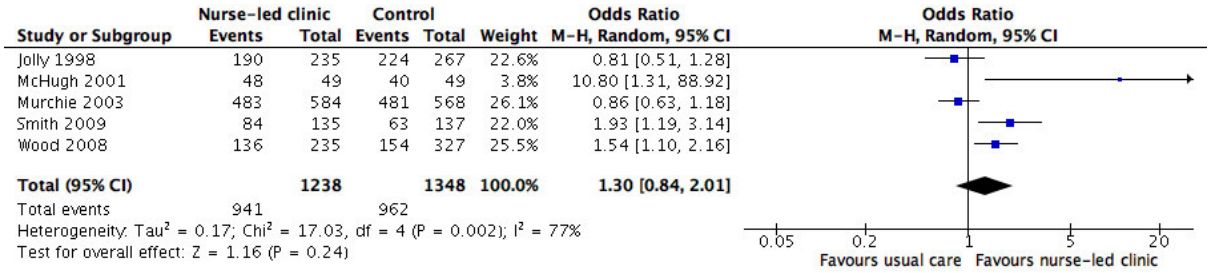
3.15 Health Behaviour

Eight trials[6,8,14,17,78 81] provided self-reported measurements of health behaviour in addition to the six[25 27,30,33,82] in the previous review. The data were presented both as continuous and dichotomous outcomes revealing consistent results. The range of outcomes varied across trials and have been grouped into the following categories: smoking, fasting blood sugar, physical activity, BMI, weight and waist circumference.

3.15.1 Smoking

For studies that addressed smoking as one of the major modifiable risk factors for cardiovascular diseases, the meta-analysis demonstrated no significant difference between the groups in supporting smoking cessation and abstinence in CHD patients (OR 1.30; 95% CI, 0.84 to 2.01; P=0.24, 5 studies, 2586 participants) (Figure 18). The absolute effect on smoking showed that among those patients who attended NLCs, 56 fewer patients per 1,000 remained abstinent from smoking compared to usual care (SOF 4). Individual studies, not pooled in the meta-analysis, showed no statically significant differences in smoking cessation rates, except one small study[25] that had higher proportions of smoking cessation in NLCs at the 12-month follow-up (Table 4). The evidence is of moderate certainty due to substantial heterogeneity I^2=77%, wide confidence intervals and uncertainty about the magnitude of effect.

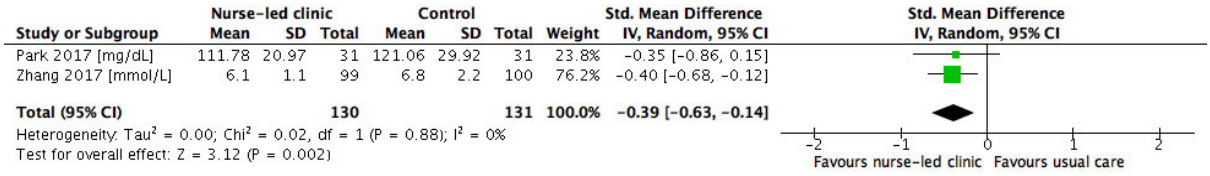
Figure 18 Effect of nurse-led clinics on smoking cessation in the long-term



3.15.2 Fasting blood sugar

There is a direct correlation between cardiovascular disease and hyperglycaemia.[84] Meta-analysis of two studies with 261 participants (Figure 19) showed that patients attending NLCs are more successful in controlling blood glucose levels in the long term than usual care (SMD=-0.39, 95% CI -0.63 to -0.14, P=0.002, two studies, 261 participants). The evidence is of moderate certainty due to the small sample size.

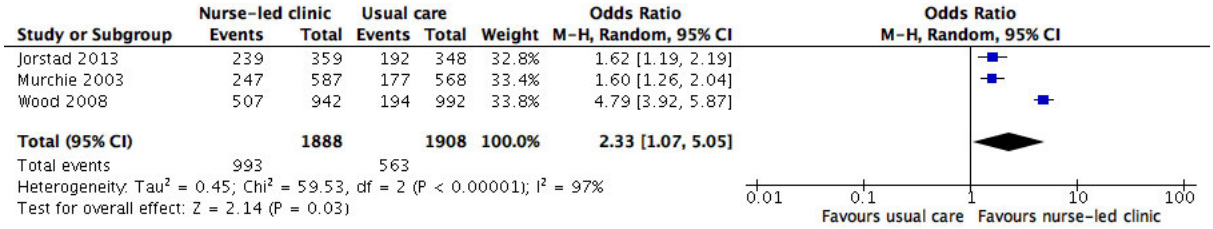
Figure 19 Effect of nurse-led clinics on fasting blood sugar in the long-term



3.15.3 Physical activity (>30 min ≥ 4x a week)

Physical activity plays an important role in survival and recovery (e.g. cardiac rehabilitation) of post-cardiac events and is correlated with fewer readmissions and decreased mortality.[85] In order to achieve the physical activity target, patients are encouraged to have 30-45 minutes of moderate-intensity activity at least four to five times a week.[15] Realistic goals should be developed, considering functional capacity and existing physical activity patterns. There was a significant increase in the odds of undertaking at least 30 minutes of physical activity four or more times a week among patients attending NLCs at the 12-months follow-up (OR 2.33; 95% CI, 1.07-5.05; P<0.00001, three studies, 3796 participants) (SOF 4).

Figure 20 Effect of nurse-led clinics on maintaining physical activity at least >30 min > 4x a week in the long-term



3.15.4 BMI

There are different findings on reducing body mass index in continuous and dichotomous data. There was slight reduction in reducing BMI (OR -1.00; 95% CI, -2.05 to -0.05; P=0.06, 2 studies, 172 participants) (Figure 21) and achieving targeted BMI (OR 1.04; 95% CI, 0.55 to1.99; P=0.9, 2 studies, 2642 participants) (Figure 22) among patients receiving care in NLCs, compared to usual care.

Figure 21 Effect of nurse-led clinics on reducing body-mass index in the long-term (continuous data)

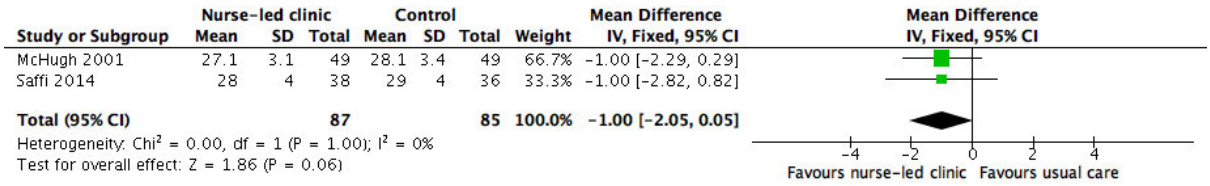
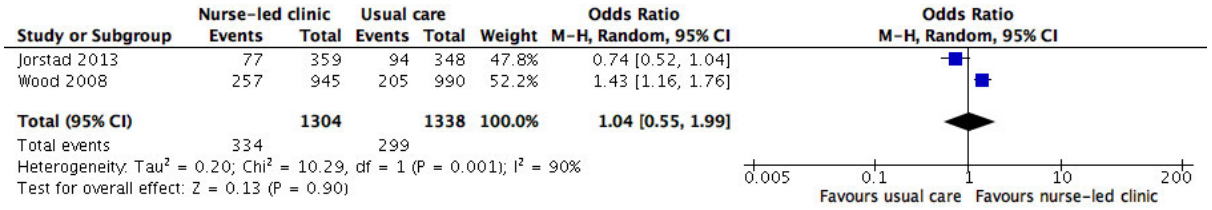


Figure 22 Effect of nurse-led clinics on achieving targeted body-mass index in the long-term (dichotomous data)



3.15.5 Weight and ideal waist circumference

Meta-analyses suggested there is no difference between NLCs and usual care in decreasing body weight (OR -1.16; 95% CI, -3.77-1.45; P=0.39, 2 studies, 493 participants) (Figure 23) and achieving ideal waist circumference (OR 1.07; 95% CI, 0.66-1.75; P=0.78, 3 studies, 3262 participants) (Figure 24) in the long-term. No statistically significant effect was observed

on patients' lifestyle changes and behaviours to reduce body weight and achieve optimal waist circumference.

The evidence of physical activity, BMI, and weight are of low to moderate certainty due to the small sample size, a small number of events, serious imprecision, and heterogeneity (SOF 4, Summary of Findings).

Figure 23 Effect of nurse-led clinics on weight in the long-term

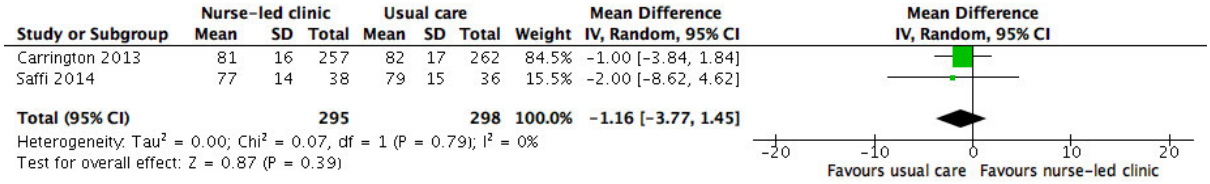
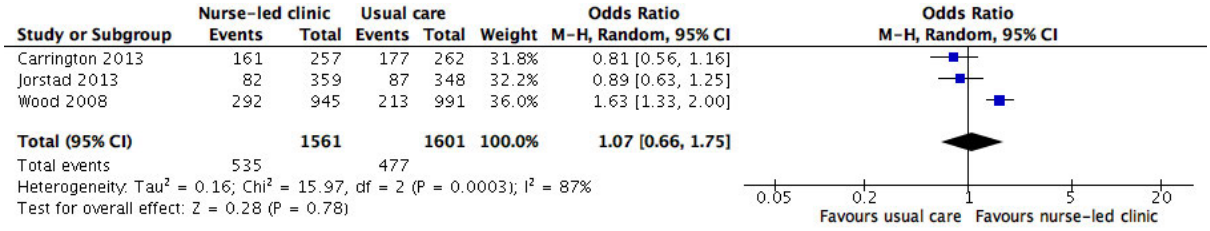


Figure 24 Effect of nurse-led clinics on achieving ideal waist circumference in the long-term



3.16 Self-Management/Treatment Adherence

3.16.1 Medication adherence

Medication adherence, defined as the willingness to follow a treatment regimen, was evaluated in six studies[6,8,21,27,30,80] with follow-up over 12 months. Compliance with treatments included prescription of cardioprotective drugs such as ACE-inhibitors, beta-blockers, diuretics, antiplatelet and lipid-lowering medications (statins).

A meta-analysis was not possible for short- and medium-term measures (3-6 months). Data from two studies (Jorstad et al. 2013[8] and Lapointe et al. 2006[21]) (Table 5) for these follow-up periods showed no significant medication adherence.

The meta-analysis at the 12-month follow-up suggests little or no difference in long-term medication compliance in patients attending NLCs over usual care for any of the cardiac

drugs: ACE-Inhibitors (OR 1.08; 95% CI, 0.75-1.56, P=0.68; 3 studies, 3158 participants) (Figure 25), antiplatelets (OR 1.31; 95% CI, 0.83-2.07; 4 studies, 4295 participants) (Figure 26), beta-blockers (OR 1.01; 95% CI, 0.69-1.49; 3 studies, 3158 participants) (Figure 27), statins (OR 1.33; 95% CI, 0.82-2.15; 6 studies, 5617 participants) (Figure 28), or diuretics (OR 1.23; 95% CI, 0.80-1.88; 2 studies, 1222 participants) (Figure 29). Evidence of certainty is low to moderate due to substantial heterogeneity of 56-92%, widely differing estimates of treatment, wide confidence intervals, small sample size and a small number of events (SOF 5).

Figure 25 Effect of nurse-led clinics on adherence to ACE-Inhibitors in the long-term

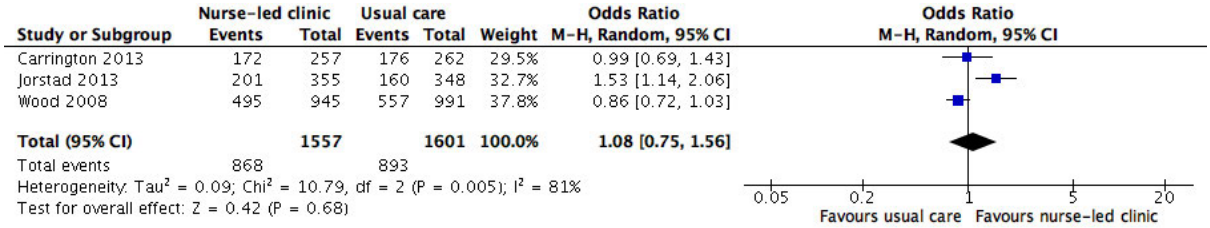


Figure 26 Effect of nurse-led clinics on adherence to antiplatelet drugs in the long-term

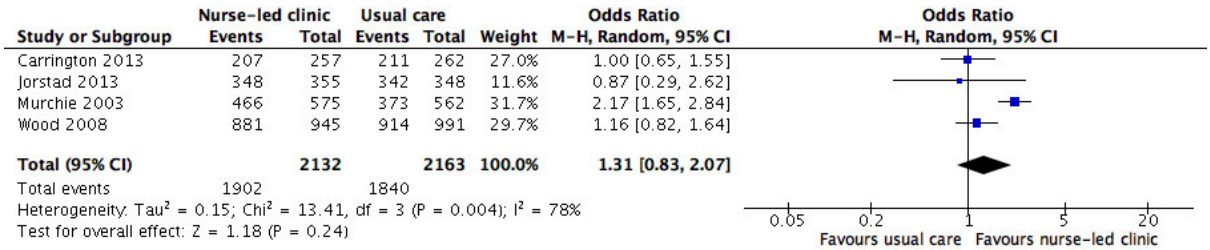


Figure 27 Effect of nurse-led clinics on adherence to beta-blockers in the long-term

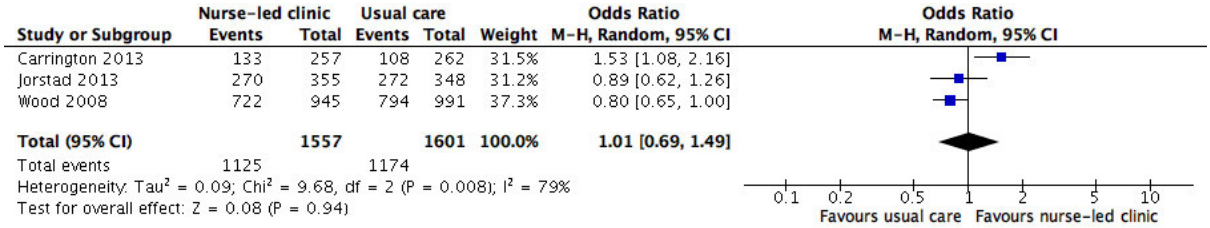


Figure 28 Effect of nurse-led clinics on adherence to statins in the long-term

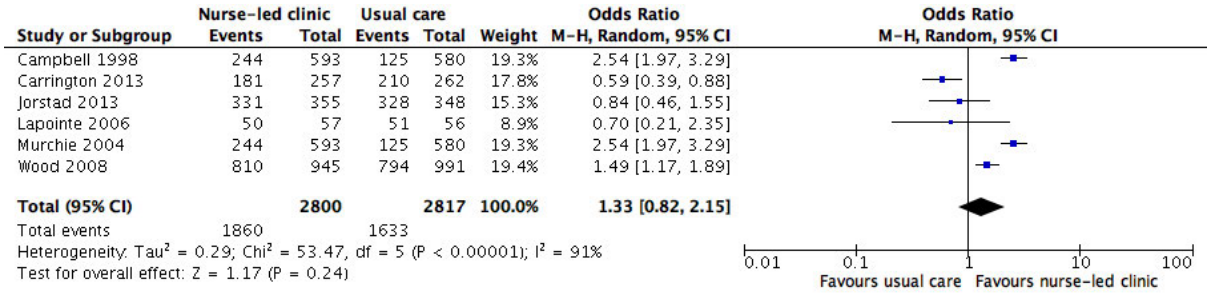
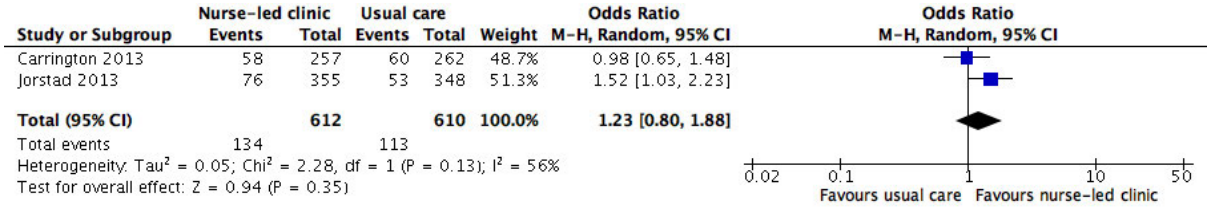


Figure 29 Effect of nurse-led clinics on adherence to diuretics in the long-term



3.17 Health Status and Health-Related Quality of Life

Health-related quality of life (HRQoL) questionnaires are used in clinical and research settings to explore the impact of healthcare on life quality.[86] One of the most widely used HRQoL questionnaires is the short form-36 (SF-36®) Health Status Survey, which presents assessments of physical and mental wellbeing.[87] Most studies included in the meta-analysis used the Short Form 36 (SF36) questionnaire to assess outcomes on health status and perceived quality of life with scores ranging from zero to 100, with the higher score indicating better outcomes, improved quality of life and less mental or physical disability.

Ten trials[5,6,8,10,11,14,17,20,78,79] in addition to the five from the previous review [25 27,31,32] provided self-reported measurements of quality of life for cardiac patients. The range of sub-outcomes varied across trials and can be grouped into three categories: physical health, mental health, depression and anxiety. Findings for each of these categories are presented below.

3.17.1 Physical health

The results of the meta-analyses of the physical domain of SF-36 showed that NLCs had no effect on physical health after the 3- and 6-months follow-up periods (MD = 0.50; 95% CI -2.30 to 3.30; P=0.73; two studies, 145 participants), (Figure 30) and (MD=2.67; 95% CI -1.06 to 6.40; P=0.16; three studies, 336 participants) (Figure 31). This may have some impact on the physical function of the quality of life in CHD patients over the long-term of 12-24 months

treatment period (MD=0.22, 95% CI 0.03 to 0.40; five studies; P=0.06; 1932 participants) (Figure 32). While there is a borderline significant effect at 12-24 months, this period shows the highest I^2 of 62%, representing moderate to substantial heterogeneity (low-quality effect) in comparison to low heterogeneity of 31% and 23% in short- and medium-term interventions. This may be due to the incongruences of the intensity of physical activities in the groups as well as disparities in health care systems in different countries. The evidence is of low to very low certainty due to the high risk of bias, a small number of events and wide confidence intervals.

Figure 30 Effect of nurse-led clinics on physical health in the short-term

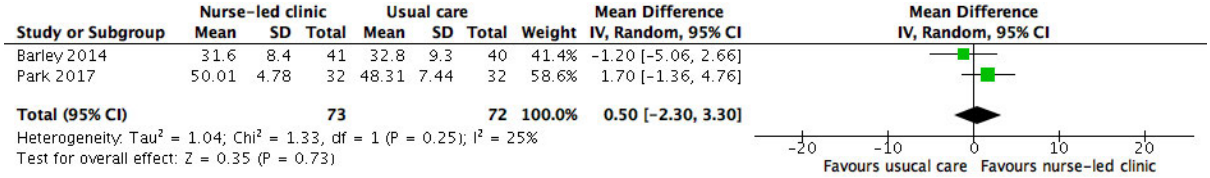


Figure 31 Effect of nurse-led clinics on physical health in the medium-term

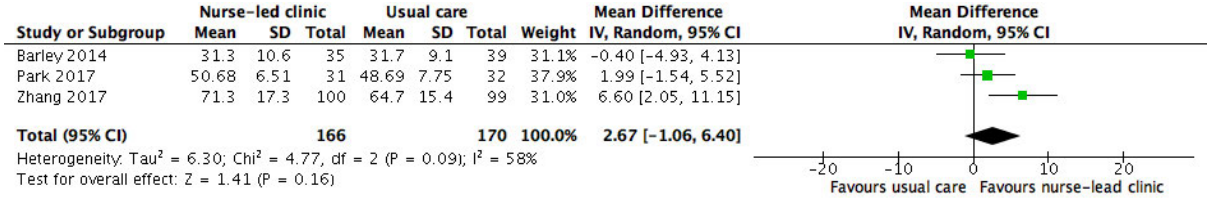
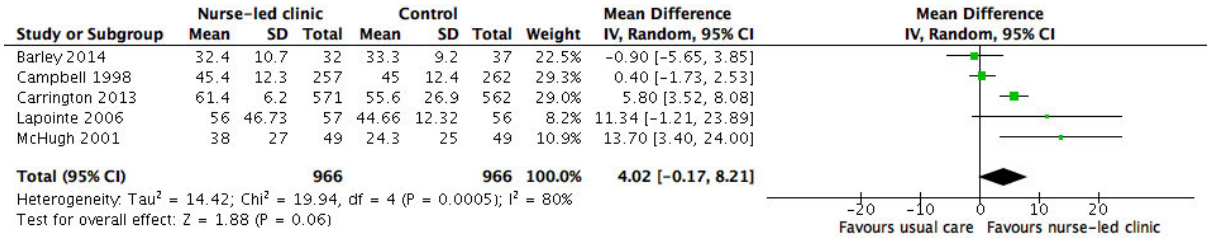


Figure 32 Effect of nurse-led clinics on physical health in the long-term



3.17.2 Mental health

Meta-analyses for the mental health domain measured by the SF-36 questionnaire suggest that cardiac NLCs, compared to usual care, lead to similar outcomes for short-, medium- and long-term follow-up periods. Mental health was reported as an outcome in the previous review as well which had similar results as the update which was not improved by attending NLCs. At the 6-week follow-up, there were no statistically significant differences between groups (MD = 2.04, 95% CI -1.23 to 5.32; P=0.22; two studies, 145 participants) (Figure 33).

The effect size was also not significant after the 6-month follow-up (MD = 3.51, 95% CI -2.28 to 9.30; P=0.24; three studies, 349 participants) (Figure 34) and after the 12-month follow-up (MD = 3.23, 95% CI -0.41 to 6.86; P=0.08; five studies, 1931 participants) (Figure 35). Significant heterogeneity of 80% and 84% in the medium- and long-term follow-up, respectively, may be attributed to the clinical variations in intervention intensity. The evidence is of low certainty due to the high risk of bias and wide confidence intervals.

Figure 33 Effect of nurse-led clinics on mental health of quality of life in the short-term

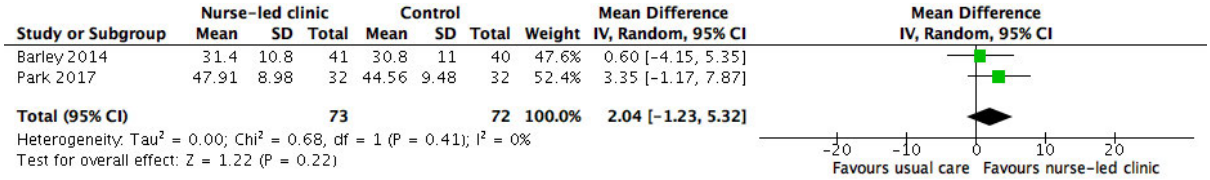


Figure 34 Effect of nurse-led clinics on mental health of quality of life in the medium-term

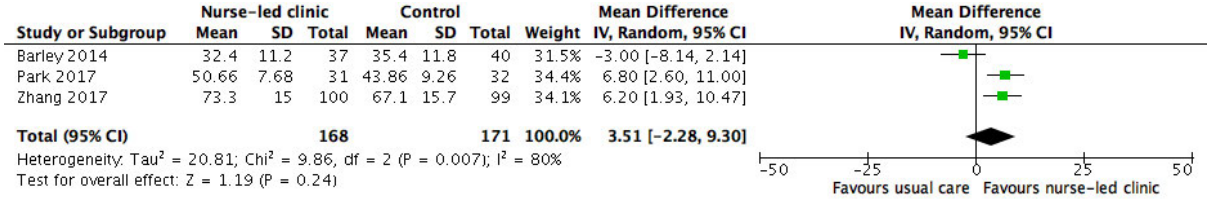
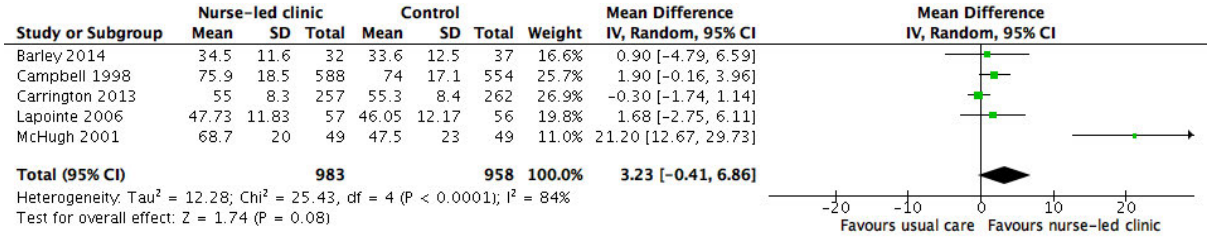


Figure 35 Effect of nurse-led clinics on mental health of quality of life in the long-term



3.17.3 Physical and mental health component summary

Meta-analysis of the physical and mental health component of SF-36 demonstrated that there was a significant difference in the physical health component in the intervention group attending the NLC at the 6-month follow-up (MD 2.56, 95% CI 0.60 to 4.52; P=0.01; three studies, 414 participants) (Figure 36). Conversely, not in the mental health component (MD 3.32, 95% CI -7.64 to 14.28; P=0.55; two studies, 333 participants) (Figure 37). The evidence is of low certainty due to substantial heterogeneity.

Figure 36 Effect of nurse-led clinics on physical component in the medium-term

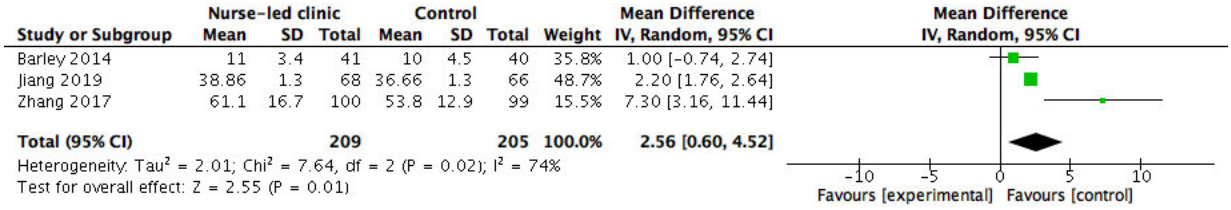
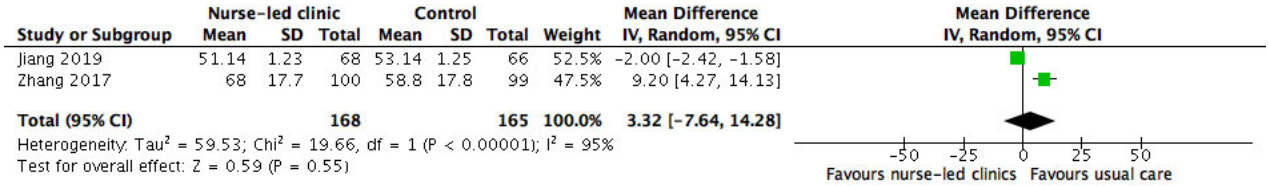


Figure 37 Effect of nurse-led clinics on mental component in the medium-term



3.17.4 Depression and anxiety

Three different tools assessed depression and anxiety: Aroll Tool, Beck's Depression Inventory Score, Hospital Anxiety and Depression Score. The meta-analyses of both continuous and dichotomous data suggest that there is no difference between NLCs and usual care in the likelihood of improving depression and anxiety in cardiac patients. Three studies with 1733 participants (SMD 0.47; 95% CI, -0.48 to 1.41; P=0.33) (Figure 38) and five studies with over 1300 participants (OR 1.27; 95% CI, 0.93 to 1.72; P=0.13) (Figure 39) were consistent in their results. The evaluation of the outcomes in the studies where meta-analysis was not possible showed no difference between the groups at any follow-up period (Table 6). The evidence was of moderate certainty due to substantial heterogeneity in continuous data and widely differing estimates of treatment effect.

Figure 38 Effect of nurse-led clinics on depression and anxiety in the long-term

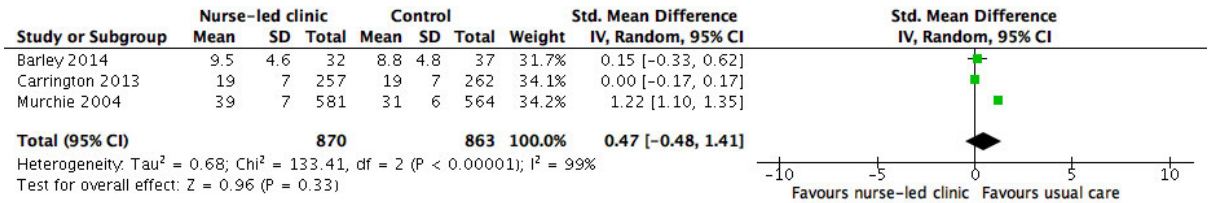
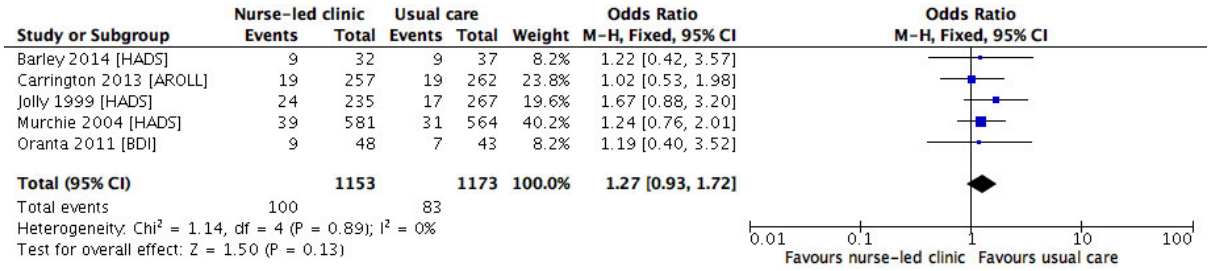


Figure 39 Effect of nurse-led clinics on depression and anxiety in the long-term



3.18 Discussion

3.18.1 Summary of the main results

This updated SR identified 16 new publications from 12 randomised trials in addition to the 13 publications included from the 2010 review[2] evaluating the effect of NLCs for patients with CHD. As demonstrated in the 2010 review, nurse-led interventions have focused on health promotion through chronic disease management, psychosocial assessments of patients' counselling and education. In addition to the treatment of risk factors, health behaviours and health-related quality of life as discussed in the 2010 review, this update identified more studies which facilitated meta-analyses on outcomes such as, all-cause mortality, chest pain exacerbations, including those requiring medical treatment, cardiac risk factors such as high BP and high cholesterol, and medication adherence according to clinical guidance. Thus, this review adds new evidence on a broader range of outcomes for cardiac patients attending NLCs.

This review identified a number of recent studies[5,6,9 11,17,20] with depression and anxiety as outcomes that contribute to CHD. A few decades ago, the main focus on risk factors for cardiac patients was primarily on lipids, hypertension and smoking cessation, while currently, there has been a growing emphasis on the significance of psychosocial factors in this population like depression, stressful life and anxiety that have recently been recognised as independent risk factors for patients with CHD.[88] Another difference compared to the 2010 review, which excludes telehealth, is that this update included seven studies[5,7,10,11,14,19,20] that utilised telehealth as a component of NLCs. However, there is no data presented to potentially explain to what extent information technology impacts the success of the intervention. That may be investigated in a subsequent study.

Findings of the meta-analyses suggested that care provided in NLCs in which the nurse collaborates with a multidisciplinary team, in comparison to care provided by doctors alone, may lead to similar, if not better, health outcomes. Whereas studies reporting outcomes associated with patient satisfaction and utilisation of services were not included in this review due to a lack of studies, there are six main outcomes reported in the current review.

All-cause-mortality

The meta-analysis indicated that NLCs might slightly reduce all-cause mortality among patients with CHD compared to usual care. Though not significantly different from usual care, the odds of all-cause mortality in the long term were 22% lower in the NLCs than in usual care. This reflects the findings of another SR on the effectiveness of NLCs on mortality and morbidity in patients with cardiovascular diseases.[66] Addressing risk factors, health behaviour and medication adherence at NLCs may contribute to lower mortality. The present review has identified some improvements for cardiac risk factors and health behaviour in the intervention group but not for medication adherence.

Exacerbation of chest pain

Chest pain is the most common presenting manifestation of acute coronary syndrome.[89] It has a considerable bearing on patients' mental wellbeing, health-related quality of life, and use of healthcare resources.[90] It can have potentially serious complications; thus, the significance of the cardiac nurses in assessing patients with chest pain and treating them cannot be underestimated.[91] Although based on only two studies, the meta-analysis showed that NLCs might lead to slightly fewer exacerbations of chest pain (53 fewer patients per 1,000 people experienced exacerbations) compared to usual care. As chest pain can be caused by cardiac anxiety and fear of body sensations,[90] nurses may prevent exacerbation of chest pain by educating patients on the way they identify, interpret, and act on chest pain symptoms.

Cardiac risk-factors

Management of CHD aims at risk assessments and prevention of chronic disease progression. Thus, early identification of modifiable cardiac risk factors, including hypertension and hypercholesterolemia, can considerably slow the development of CHD.[78] This review yielded mixed results. Regarding achieving BP targets, outcomes in this review

demonstrated significant differences between NLCs and usual care in achieving the targeted systolic and diastolic BP in the medium- and long-term follow-up periods with the NLCs performing better than usual care. In NLCs, 92 more patients per 1,000 people maintained systolic BP of <140 mm Hg and 48 more patients per 1,000 people maintained diastolic BP <90 mm Hg over the period of 12 months. This is consistent with the results of a review on the effectiveness of nurse-led multifaceted and targeted interventions in cardiac risk factor reduction in adults with established cardiovascular diseases.[92]

The review examined 18 trials undertaken in the UK and Australia, which combined multifaceted interventions involving health assessment, health education, motivational interviewing, counselling and management of cardiac risk factors, and targeted interventions aimed at achieving changes in a specific risk factor. The review specifically included trials on risk factor reduction, and improvements in BP were exhibited in most trials that employed multifaceted interventions. A positive impact on 10-year cardiovascular risk was also reported. The authors of this review attributed the success of nurse-led care to being systematic, methodical and regular with continuous encouragement to change behaviour patterns, promoting greater commitment and better clinical outcomes.[92] Another trial[16] showed that increasing patients' knowledge of CHD and improving their awareness of the risk factors, and providing practical steps for modifying them, empowers the participants to become more involved in self-care activities, which demonstrates that empowerment and motivation appear to be important components of NLCs.

The results of the present review on blood lipids suggested that NLCs could not achieve the target level of total cholesterol ≤4-4.5mmol/L and increase HDL-C concentrations more effectively than usual care. These results were similar to the ones in the review on cardiac risk factor reduction in adults[92] that failed to demonstrate statistically significant reductions in serum cholesterol in the intervention group.

Health behaviours

This review highlights that lifestyle interventions provided in NLCs are generally effective and lead to changes in physical activity and blood sugar management. However, these modifications are not sustained over 12 months. The included studies also identified difficulties in improving health behaviours in CHD patients, particularly smoking cessation

and body weight reduction. In contrast, a smoking cessation intervention in CHD patients substantially decreased mortality risks and other cardiac risk factors according to a Canadian study.[14] Although interventions on smoking cessation based on advice in the EUROACTION programme decreased the risk of relapse in CHD patients; it did not have an impact on high-risk patients.[15]

Improvement of lifestyle behaviour in patients with CHD patients around physical exercise and body weight reduction is a crucial part of nurse-led interventions for patients with CHD. There was a significant increase in adequate physical activities (at least 30 minutes for 4 or more times a week) among patients attending NLCs in three trials and fasting blood sugar in two trials. Despite this, nurse-led care may lead to little or no difference in achieving targeted body mass, weight loss, and ideal waist circumference in the long term. The lack of observed effect on body weight and achieving optimal body mass index corresponds to the results of another review[58] summarising evidence on the adherence to dietary recommendations and weight control in the nurse-led intervention group at the 12-month follow-up. Despite adding new studies, findings on exercise/body weight have not changed since the last review conducted 11 years ago, which highlights the challenges of changing and maintaining healthy behaviours.

Similar to the findings of the present review, another review of 12 trials in Western and Asian countries on nurse-led patient-centred care for behavioural risk modification[58] showed no significant long-term effects on improving patients' behavioural risks at two years after MI. The review that analysed behavioural risks, health-related quality of life and cardiac physiological parameters showed that none of the included studies reported significant effects on improving the behavioural risk of the patients with CHD except one study that showed improvement in dietary adherence.

Self-management

Cardioprotective drugs are a primary therapy for cardiac patients. However, adherence remains suboptimal, resulting in inadequate control of symptoms and increased risk of future events, including readmissions to hospital and death.[93] Evidence shows that patients' commitment and full adherence to treatment according to guidelines for the management of atherosclerosis, angina, and MI has been associated with reduced rates of adverse events.[94]

Little or no difference was found in long-term medication compliance in patients attending NLCs or usual care for cardioprotective drugs such as ACE-inhibitors, beta-blockers, diuretics, antiplatelets, and lipid-lowering medications (statins). A significant difference in adherence to cardio-protective drugs between NLC and usual care was noted only in statins in three trials,[27,31,80] which resulted in improved blood cholesterol concentration in the intervention group. Prescription of lipid-lowering agents was high in both groups, while the majority of patients used antihypertensive drugs, whereas ACE-inhibitors were the most prescribed drug.

The findings of another review on cardiovascular medication adherence among cardiac patients demonstrate that medication adherence may be best achieved when the nurse-led intervention is multifaceted and includes behavioural and educational interventions comprising text and mail messages, telehealth and motivational interviewing, counselling and education.[93] The review, which compared various types of interventions used by healthcare providers, suggested that the most-promising interventions are those that utilise multiple approaches and aim to change the desired behaviour. The health benefits of medications can be maximised with the help of technology like automated phone text messages that reinforce behaviours and adherence to medication schedules.[93] In this review, a number of trials included additional telephone coaching and telephone education for chronic disease management, which has been implemented more efficiently in times of the COVID-19 pandemic.

Health status and quality of life

Meta-analyses on health status and health-related quality of life revealed mixed findings that could be caused by heterogeneity in the characteristics of the studies. Results of the SF-36 did not reveal any significant improvement in physical and mental health domains for short-, medium- and long-term follow-up periods, although effects tended to strengthen as follow-up time increased. A recent review on secondary prevention of CHD modifications showed no significant long-term beneficial effects on improving patients' mental and physical health.[58] This result may be related to the patients' and health professionals' perception of the attainability of the goals that may impact their adherence to a long-term care plan bearing in mind potential changes in the course of cardiac disease. As people with CHD often experience complications in the course of their disease and progressive changes in their

health conditions, it may impact their self-efficacy, health outcomes and overall quality of life.[58]

When depression is prevalent after MI and CHD, it may decrease quality of life, function and well-being[20] and add to cardiac morbidity and mortality.[10] Depressive disorder is correlated with main cardiac events with a relative risk of 2.69.[95] Longitudinal studies have revealed that depression can remain many months after the acute episode of CHD and may result in a major loss of functioning in excess of what is anticipated from the disease itself.[95] In recent years, more trials have focused on psychological outcomes and improving the mental well-being of patients with CHD. This review identified seven studies that included depression and anxiety as one of the outcomes. Including mental health care in NLCs would constitute a major improvement in present care, as depression management has not been routinely included in this population.[5]

Treatment of depression in cardiac patients may improve their quality of life.[95] However, NLCs did not seem to improve depression and anxiety, as no difference in changes were found between the groups during long-term follow-up. These results are consistent with the SR by Luo et al.[96] that evaluated psychological outcomes among patients assigned to Nurse-Led Programs of Support and Management and showed no improvement in mental well-being, particularly depression and anxiety among CHD patients. Although there was a significant reduction in depression levels in another integrated nurse-led prevention program on cardiovascular diseases, which lasted over a 6-month period, the results were not maintained after 1 year.[97] As depressed patients appear to be less likely to adhere to cardiac programs[88], this may also affect the recurrence/worsening of the condition, as well as their health behaviour, it is of great significance to detect, diagnose and provide depression treatment and focus on participation and compliance with interventions which enhances the urgency of implementing depression interventions in NLCs.

3.19 Implications for Practice

This review provides evidence of the effectiveness of NLCs in selected outcomes; therefore, NLCs can play a significant role when providing care to patients with CHD, and their establishment within health systems should be further explored. Since patient outcomes from

attending NLCs are equal to or better than usual care, NLCs could become routine models of care for patients with CHD. Some trials have introduced telehealth components in the intervention, so NLCs could be beneficial for remote communities, with evidence from some recent trials that telehealth can be offered via NLCs.[98 102]

Coronary heart disease and depression have known to have an adverse effect on each other, imposing severe burdens and suffering.[103] Anxiety and depression are diagnosed in 20–30% of patients with heart disease, and up to 43% in the first 12 months after an acute cardiac event.[104] The findings of this review demonstrated modest results in reducing moderate to severe depression and anxiety in CHD patients. A worse quality of life and a higher incidence of adverse events have been observed in CHD patients with a history of depression compared to non-depressed patients.[105] Poor results in reducing moderate to severe depression and anxiety in CHD patients indicate the importance of bringing proactive depression screening and referral after a cardiac event into NLCs. Providing a comprehensive treatment should assist in identifying patients who are at risk of poor prognosis and mortality. Further referral to a psychologist is recommended during the initial assessment. If there is no psychologist routinely working with NCLs, it would be recommendable to add one to the MD team on the site.

The benefits of early detection and treatment of depression in patients with CHD include an enhanced quality of life, improved compliance, and potentially better cardiac outcomes. New treatment approaches should be developed and examined to achieve better psychological outcomes in patients who attend NLCs. Collaborative approaches in the care of depression will be required to improve mental health-related quality of life in cardiac patients, decrease the severity of depression, and improve adherence to the management of cardiac risk factors.

3.20 Implications for Future Research

For the last two years, COVID-19 has had a profound impact on the healthcare system around the world and transformed its delivery in the community and clinics. In the context of the current global situation with the COVID-19 pandemic, social isolation and distancing measures are in place to prevent the spread of the disease and lessen potential harm to cardiac patients. COVID-19 pandemic has presented unique challenges to healthcare, and

telehealth has developed as an indispensable technology to safely and efficiently deliver healthcare to patients.[106] Telehealth offers a pathway to connect with the clients to attend to their issues with the use of technology instead of conventional face-to-face consultation.[101]

Future research on telehealth in NLCs is recommended to establish consumer acceptance as well as efficient and cost-effective ways to deliver nurse-led care remotely. There is a need to focus on telehealth and other innovative care models, which are now becoming an essential component of providing outpatient care. Future research is needed on the level of training the nurses should undertake to assume the extended scope of duties in NLCs. This update showed a broad variation in nurses' qualifications, duties and training. Most of the nurses in the trials included in this review had master's degrees or were qualified to work in cardiovascular care as well as additional training in the speciality prior to the trial. While nurses internationally and in Australia may have adequate qualifications to work in NLCs, the Australian medical profession voices concern to support NLCs. According to the position statement of The Royal Australian College of General Practitioners (RACGP), nurses do not have sufficient training needed to practice in an open setting with patients presenting with a wide range of health issues.[107] As traditional nursing training focuses on the standard diagnosis, nurse-led care may encounter atypical serious conditions that are beyond their nursing expertise level that may not be well managed at the clinic.[107] The RACGP argues that nurses generally are not educated to oversee patients with complex co-morbidities, so mismanagement could possibly cause harm to patients.[107]

Cost-effectiveness could be further investigated, as a few studies have different health economic outcomes.[41,108 110] Some studies report that NLCs appear to be more cost-effective compared to a usual care-comparator, which can impact the policy direction about the delivery of cost-effective services, as they represent value for money.[110] Conversely, the RACGP states that '…nurses rely on decision-making algorithms' in their clinical setting, depending on their experience, which may increase health expenditure by generating a higher number of tests and referrals to specialists and prescribing more medications.[107] These higher investigative costs can prevent follow-on costs from missed prevention. A large cost-benefit-analysis may assist in identifying this area of the economic value of NLCs.

Further research is recommended on measuring patient satisfaction, which was not possible to synthesise in this review. Patient satisfaction, one of healthcare's major quality measurements, promotes patient enablement, which in turn affects patients' ability to manage their lifestyle and health behaviours.[38] Cross-sectional studies on patient satisfaction in NLCs for patients with chronic cardiac and kidney diseases demonstrated that patients were generally satisfied with NLCs in the management of their chronic conditions.[38,111] Furthermore, since CHD is a complex disease with different stages during the life course, it would be interesting to research at what stages of the disease patients are most responsive to nurse-led care. For example, by comparing those patients who are medically (as opposed to surgically) managed, patients before or after the surgery, newly diagnosed patients or those who have lived with CHD for a considerable time.

Further studies should be conducted to research barriers and enablers for the successful establishment of NLCs, as well as other factors that will make this model of care provision effective for patients and nurses. Further research is also recommended to explore and evaluate the economic impact and cost-effectiveness of NLCs. The educational and training level of nursing staff required to manage extended responsibilities in the clinics should be appraised.

3.21 Limitations

This review has several limitations. Meta-analysis for some outcomes included only 2-3 studies, and some trials only had a small number of participants, making it difficult to make strong recommendations when confidence intervals for effect sizes are wide. However, this has been accounted for in the meta-analyses and through the GRADE assessment. Not all included studies reported long-term outcomes; thus, some meta-analyses were carried out only for short- or medium follow-up periods. *Given that telehealth was included as an additional setting in NLC and was excluded in the original review, the studies prior to 2010 have not been searched for telehealth.* Databases in the English language only were searched; thus, relevant non-English trials were excluded. Not all the data could be retrieved from all the included studies, as the contacted authors did not provide the requested data.

3.22 Conclusion

The evidence of this review suggests that NLCs can play a significant role in providing care to patients with CHD and may have similar or better effects on the prevention and treatment of CHD compared to usual care. The trials added to this review included outcomes such as all-cause mortality, exacerbation of chest pain and adherence to medication that were not presented in the 2010 review. The current analysis suggested a likely favourable effect of NLCs on mortality and chest pain, some cardiac risk factors, increase in physical activities, but effects on transformations of some health behaviours, compliance to medications and health-related quality of life were less evident. Nevertheless, the evidence shows that NLCs provide a model of care that is at least as effective as usual care for patients with CHD.

3.23 Funding

No funding was received to undertake the review.

3.24 Conflicts of Interest

The authors did not have any potential conflict of interest or any personal, professional or financial bias in this review project.

Chapter 4 General Discussion and Conclusion

4.1 Discussion

This thesis presents a SR on the effectiveness of NLCs for patients with CHD. This chapter discusses the findings in light of currently available evidence and provides implications for clinical practice and future research. While the findings of the SR were discussed in light of the global literature, the discussion here explores NLCs in Australia, including nurse-led services that are available nationwide, the policies on NLCs in Australia, and support from the medical organisations, and highlights the potential for NLCs remote Australia.

With the increased longevity of the population and treatment complexities of chronic diseases, the health care needs have altered globally.[112] Health systems must develop innovative ways to address these challenges, including incorporating the full capacity of nurses in the healthcare workforce.[113] Nurse-led clinics may have the design to meet these challenges and are already established both nationally and internationally in healthcare with favourable benefits of decreased hospital readmissions, improved clinical and patient outcomes, and increased accessibility in remote areas.[114] Improved utilisation of the nursing workforce in healthcare is crucial if Australia is to effectively meet increasing health demands and contribute to reducing the burden on the healthcare system.[114] Governments are major stakeholders in healthcare and are responsible for regulatory, policy and implementation to improve the healthcare system and population well-being.

In 2012 Hoare et al. undertook a realist review on the role of Government policy in supporting nurse-led care in general practice. They examined NLC clinical governance and practice in three developed countries: the UK, New Zealand and Australia. While practice nurses operate NLCs autonomously, managing patients with chronic conditions in the UK and other countries, there is limited existing evidence that nurses in Australia and New Zealand routinely deliver NLCs in primary care. The nurse workforce in England has both a clinical governance and a Quality and Outcomes Framework indispensable for NLCs management. Comparatively, Australia and New Zealand have no career structure for practice nurses.[115] The main motivation for expanding nurse-led care in the UK was financial incentives to attain affirmative patient health outcomes. However, Australia and New Zealand have lacked similar plans to cultivate the primary care nursing workforce and initiate a national quality

framework with financial incentives for NLCs. The current situation may not be sustainable in the long term due to the increasing numbers of patients with chronic conditions.[115]

Nurse-led clinics are expanding in a diverse range of specialities in Australia in response to the restructuring of healthcare services. In the last ten years, there has been an increase in NLCs. A scoping study on nurse-led services in Queensland stated that NLCs are "the sleeping giant of healthcare reform in Australia" (p. 363), and the time has come for changes in policy to fulfil the potential of NLCs.[116] The findings of the review demonstrated that nurses had become leading teams in hospitals and communities, providing accessible service to patients with chronic diseases.[116]

In an Australian setting, a nurse-led chest pain clinic in Royal Hobart Hospital proved to have a more efficient patient assessment compared to a general cardiology clinic and superior clinical outcomes to the usual care.[117] An atrial fibrillation (AF) clinic in The Canberra Hospital, established in 2015 as a pilot NLC, demonstrated effectiveness in improving adherence to anticoagulation guidelines for the management of AF patients.[118] An NLC in a tertiary hospital in Australia designed to prevent progressive cardiac dysfunction and heart failure (HF) was associated with decreased hospital stay and improved cardiac function over the long term.[119] As these publications have their limitations, such as different population sources in the comparative groups, the absence of a control group with standard care, and a small heterogenous cohort, it is worthwhile to undertake further studies and assess to what extent NLCs are effective in managing risk factors compared to other models of care.

4.1.1 Expansion of NLCs in Australia

Although there is a great potential for NLCs in Australia, strategic nursing leadership and planning are required. Nurses can actively promote policy transformations that substitute a system focused on acute and chronic care with services that are positioned around patient-centred care.[116] Further studies should be conducted to research barriers and enablers for the successful establishment of NLCs as well as other factors that will make this model of care provision effective for patients and nurses.

There is a perspective that the implementation of NLCs will accelerate, as they have proved to be an evidence-based remedy to manage the increased burden on the healthcare system. Expanding NLCs in Australia will require thorough planning and vigorous clinical governance structure, and support from medical colleagues. According to RACGP[107], NLCs have not received due support from medical professionals, which partially explains the lack of progress of NLCs here in Australia. RACGP does not consider NLCs to be "a long-term solution to health workforce issues", as all patients should have access to primary care led by culturally responsive GPs.[107]

Nursing education and practice would require some transformation to further develop NLCs in Australia. For example, the Commonwealth government, Australian Health Practitioner Regulation Agency (AHPRA), and health care organisations[120] could take actions to encourage and support nurses to complete advanced practice degree programs that will assist them in transitioning into innovative clinical practice areas.[120] Australian universities do offer courses and leadership programs for NPs to obtain the necessary qualification and competencies for expanded practice to work at an advanced level and gain knowledge on ethical, professional and legal issues relating to autonomous and multi-disciplinary practice. Although the number of the programs and courses continues to grow, there are still a number of limitations to the NP role in Australia. Nurse practitioners have lacked organised guidance and mentorship for their role at the local and national levels.[121] Their practice was restricted until the passing of the Health Legislation Amendment (Midwives and Nurse Practitioners) Act 2010, which has provided them with access to government-subsidised services.[121] It is crucial that beneficial policies and appropriate resources continue to support the role of NPs and other advanced nursing roles so that they are efficiently utilised in the Australian healthcare system.[121]

As this review was being conducted, unprecedented events took place in the form of the COVID-19 global pandemic, which had a huge burden on healthcare provision and expenses. The post-pandemic effects on the health system are yet to be determined. During these critical times, it is becoming more apparent that nurses are the backbone of global health care, working at the front line of hospitals, clinics, units and wards, nursing homes, and prisons, and that the need for nurses and NLCs has never been greater.[122] With healthcare systems around the world experiencing strain from COVID and its continuously

emerging new variants, unprecedented nursing shortages has presented a tremendous burden to the healthcare system.[123]

New ways of care delivery have been necessitated to continue to address patients' needs, such as telehealth care and virtual clinics. For example, the Australian Government initiated temporary funding for telehealth consultations provided by primary healthcare nurses to deliver services for the management of chronic diseases.[124]

A number of new studies [6,7,10,11,13,14,16,20] included in this update utilised telephone coaching and counselling. However, there was no data on what extent information technology was involved in NLCs and whether it contributed to the success of the intervention. Other pilot trials in this area demonstrated that virtual clinics have been suitable and can be promptly utilised in response to coronavirus.[125]

4.2 Implications for Practice

Based on the synthesis and meta-analysis of this review, NLCs are comparable to usual care that provides treatment to CHD patients; therefore, the establishment of NLCs should be further investigated. Studies have shown that NLCs may be effective in educating CHD patients in the communities, with the evidence supporting short-, medium- and long-term outcomes and reducing the re-hospitalisation burden. Nurse-led clinics provide effective tools to empower patients to actively manage their conditions. Since some trials have already utilised new technology components of telehealth in clinics, NLCs could be beneficial for remote communities. Telehealth expands patient access to services, thereby promoting the integration of remote services and primary care in supporting efficient care management.[126]

Additional focus should be on preventive variables for CHD patients, including dietary patterns, lifestyle in various cultures and countries, and ethnic and cultural beliefs towards disease should be considered when establishing NLCs in different localities.[127] Nurses' collaborative approach within multiple disciplinary care can help to steer the patient journey towards healthy choices.[38] Changes may be needed in NPs' education and specialisation to have a stronger focus on behaviour changes, as the findings of this review have demonstrated that interventions are not currently effective.

Translation of research into clinical practice can be challenging and can encounter several barriers. While nurses can be enthusiastic in responding to new reforms in healthcare and offering their services and expertise, moving towards more autonomous practice in NLCs requires adequate education and individual desire to improve provision and appropriate planning.[128] When establishing new services like NLCs, ongoing performance evaluation is critical to ensure that NLCs achieve their objectives and provide safe, high-quality services that meet patients' needs. It is a crucial element that should be approved by all stakeholders.[112]

4.3 Conclusion

Interventions of NLCs, aiming to improve health outcomes, have the potential to reduce mortality and cardiac risk factors and improve quality of life. This SR with meta-analysis offers new evidence related to the effectiveness of NLCs for patients with CHD. A sufficient number of trials were identified to undertake meta-analysis and estimate overall effect sizes for NLCs compared to usual care for patients with CHD on a range of outcomes. This updated review contributes to the body of evidence on the effectiveness of NLCs. Furthermore, it lends support to the expansion of healthcare services for secondary prevention of CHD and the advance of nursing careers in Australia as well as overseas.

References

1. Alzhanova A, Schultz T, Hendriks J, Schadewaldt V. Effectiveness of nurse-led clinics for patients with coronary heart disease. . PROSPERO; 2020 [cited 2020 4 October]. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=205270
2. Schadewaldt V, Schultz T. A systematic review on the effectiveness of nurse-led cardiac clinics for adult patients with coronary heart disease. JBI Library of Systematic Reviews. 2010; 8(2):53-9.
3. Garner P, Hopewell S, Chandler J, MacLehose H, Schünemann HJ, Akl EA, et al. When and how to update systematic reviews: consensus and checklist. BMJ (Online). 2016; 354:i3507-i.
4. Aromataris E, Munn ZE. JBI Manual For Evidence Synthesis. JBI, 2020. [cited 2018 1 June]. Available from: https://synthesismanual.jbi.global
5. Barley EA, Walters P, Haddad M, Phillips R, Achilla E, McCrone P, et al. 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. 2014; 9(6):e98704.
6. Carrington MJ, Chan YK, Calderone A, Scuffham PA, Esterman A, Goldstein S, et al. A multicenter, randomized trial of a nurse-led, home-based intervention for optimal secondary cardiac prevention suggests some benefits for men but not for women: the Young at Heart study. Circ Cardiovasc Qual Outcomes. 2013; 6(4):379-89.
7. Chan Y, Stewart S, Calderone A, Scuffham P, Goldstein S, Carrington M. Optimising secondary cardiovascular prevention in privately insured cardiac patients: The young @ heart multicentre randomised controlled trial. Heart Lung Circ. 2012; 21:S311-S2.
8. Jorstad HT, Von Birgelen C, Alings AMW, Liem A, Van Dantzig JM, Jaarsma W, et al. Effect of a nurse-coordinated prevention programme on cardiovascular risk after an acute coronary syndrome: Main results of the RESPONSE randomised trial. Heart. 2013; 99(19):1421-30.
9. Jorstad HT, Minneboo M, Helmes HJ, Fagel ND, Scholte Op Reimer WJ, Tijssen JG, et al. Effects of a nurse-coordinated prevention programme on health-related quality of life and depression in patients with an acute coronary syndrome: results from the RESPONSE randomised controlled trial. BMC Cardiovasc Disord. 2016; 16(1):144.
10. Oranta O, Luutonen S, Salokangas RK, Vahlberg T, Leino-Kilpi H. The outcomes of interpersonal counselling on depressive symptoms and distress after myocardial infarction. Nord J Psychiatry. 2010; 64(2):78-86.
11. Oranta O, Luutonen S, Salokangas RKR, Vahlberg T, Leino-Kilpi H. Depression-Focused Interpersonal Counseling and the Use of Healthcare Services After Myocardial Infarction. Perspect Psychiatr Care. 2012; 48(1):47-55.
12. Park M, Song R, Jeong JO. Effect of goal attainment theory based education program on cardiovascular risks, behavioral modification, and quality of life among patients with first episode of acute myocardial infarction: Randomized study. Int J Nurs Stud. 2017; 71:8-16.
13. Saffi MAL, Polanczyk CA, Rabelo-Silva ER. Lifestyle interventions reduce cardiovascular risk in patients with coronary artery disease: a randomized clinical trial. Eur J Cardiovasc Nurs. 2014; 13(5):436-43.
14. Smith PM, Burgess E. Smoking cessation initiated during hospital stay for patients with coronary artery disease: A randomized controlled trial. Can Med Assoc J. 2009; 180(13):1297-303.
15. Wood DA, Kotseva K, Connolly S, Jennings C, Mead A, Jones J, et al. Nurse-coordinated multidisciplinary, family-based cardiovascular disease prevention programme (EUROACTION) for patients with coronary heart disease and asymptomatic individuals at high risk of cardiovascular disease: A paired, cluster-randomised controlled trial. The Lancet. 2008; 371(9629):1999-2012.

16. Zhang P, Hu YD, Xing FM, Li CZ, Lan WF, Zhang XL. Effects of a nurse-led transitional care program on clinical outcomes, health-related knowledge, physical and mental health status among Chinese patients with coronary artery disease: A randomized controlled trial. Int J Nurs Stud. 2017; 74:34-43.
17. Corones-Watkins KM, Theobald KA, White KM. Outcomes of a randomised pilot trial of a nurse-led clinic for patients after percutaneous coronary intervention. Aust Crit Care. 2019; 32(4):285-92.
18. Karataş T, Polat Ü. Effect of nurse-led program on the exercise behavior of coronary artery patients: Pender's Health Promotion Model. Patient Educ Couns. 2021; 104(5):1183-92.
19. Jiang W, Zhang Y, Yan F, Liu H, Gao R. Effectiveness of a nurse-led multidisciplinary self-management program for patients with coronary heart disease in communities: A randomized controlled trial. Patient Educ Couns. 2020; 103(4):854-63.
20. Oranta O, Luutonen S, Salokangas RK, Vahlberg T, Leino-Kilpi H. The effects of interpersonal counselling on health-related quality of life after myocardial infarction. J Clin Nurs. 2011; 20(23-24):3373-82.
21. Lapointe F, Lepage S, Larrivée L, Maheux P. Surveillance and treatment of dyslipidemia in the post-infarct patient: Can a nurse-led management approach make a difference? Can J Cardiol. 2006; 22(9):761-7.
22. Woollard J, Burke V, Lj B. Effects of general practice-based nurse-counselling on ambulatory blood pressure and antihypertensive drug prescription in patients at increased risk of cardiovascular disease. J Hum Hypertens. 2003; 17(10):689.
23. Woollard J, Burke V, Beilin LJ, Verheijden M, Bulsara MK. Effects of a General Practice-Based Intervention on Diet, Body Mass Index and Blood Lipids in Patients at Cardiovascular Risk. Eur J Prev Cardiol. 2003; 10(1):31-40.
24. Jiang X, Sit JW, Wong TK. A nurse-led cardiac rehabilitation programme improves health behaviours and cardiac physiological risk parameters: evidence from Chengdu, China. J Clin Nurs. 2007; 16(10):1886-97.
25. McHugh F, Lindsay GM, Hanlon P, Hutton I, Brown MR, Morrison C, et al. Nurse led shared care for patients on the waiting list for coronary artery bypass surgery: a randomised controlled trial. Heart (British Cardiac Society). 2001; 86(3):317-23.
26. Khunti K, Stone M, Paul S, Baines J, Gisborne L, Farooqi A, et al. Disease management programme for secondary prevention of coronary heart disease and heart failure in primary care: a cluster randomised controlled trial. Heart. 2007; 93(11):1398-405.
27. Campbell NC, Thain J, Deans HG, Ritchie LD, Rawles JM, Squair JL. Secondary prevention in coronary heart disease: baseline survey of provision in general practice. BMJ. 1998; 316:1340-4.
28. Campbell NC, Ritchie LD, Thain J, Deans HG, Rawles JM, Squair JL. Secondary prevention in coronary heart disease: a randomised trial of nurse led clinics in primary care. Heart (British Cardiac Society). 1998; 80(5):447-52.
29. Delaney EK, Murchie P, Lee AJ, Ritchie LD, Campbell NC. Secondary prevention clinics for coronary heart disease: a 10-year follow-up of a randomised controlled trial in primary care. Heart. 2008; 94(11):1419-23.
30. Murchie P, Campbell NC, Ritchie LD, Simpson JA, Thain J. Secondary prevention clinics for coronary heart disease: four year follow up of a randomised controlled trial in primary care. BMJ (Clinical research ed). 2003; 326(7380):84.
31. Murchie P, Campbell N, Ritchie L, Deans H, Thain J. Effects of secondary prevention clinics on health status in patients with coronary heart disease: 4 year follow-up of a randomized trial in primary care. Fam Pract. 2004; 21(5):567-74.

32. Jolly K, Bradley F, Sharp S, Smith H, Thompson S, Kinmonth A-L, et al. Randomised controlled trial of follow up care in general practice of patients with myocardial infarction and angina: final results of the Southampton heart integrated care project. BMJ. 1999; 318(7185):706-11.
33. Jolly K, Bradley F, Sharp S, Smith H, Mant D. Follow-up care in general practice of patients with myocardial infarction or angina pectoris: initial results of the SHIP trial. Fam Pract. 1998; 15(6):548-55.
34. GRADEpro. GRADEpro guideline development tool [software]. 2015 [cited 2011 1 July]. Available from: https://www.gradepro.org/
35. Sanchis-Gomar F, Perez-Quilis C, Leischik R, Lucia A. Epidemiology of coronary heart disease and acute coronary syndrome. Annals of translational medicine. 2016; 4(13):256-.
36. Ralapanawa UU, Sivakanesan RR. Epidemiology and the Magnitude of Coronary Artery Disease and Acute Coronary Syndrome: A Narrative Review. J Epidemiol Glob Health. 2021; 11(2):169-77.
37. Liu JLY, Maniadakis N, Gray A, Rayner M. The economic burden of coronary heart disease in the UK. Heart (British Cardiac Society). 2002; 88(6):597-603.
38. Desborough J, Parkinson A, Korda R, Han J, McManus M, Aung E. The practical use of the Patient Enablement and Satisfaction Model in nurse-led outpatient cardiac clinics. Collegian (Royal College of Nursing, Australia). 2019; 26(4):415-21.
39. Bishop K, Dunford M, Goodwin M, Ho W, On ML, Moon L. Australian Burden of Disease Study: Fatal Burden of Disease 2010. Australian Institute of Health and Welfare; 2015. 47 p.
40. Berwick DM, Nolan TW, Whittington J. The Triple Aim: Care, Health, And Cost. Health Aff (Millwood). 2008; 27(3):759-69.
41. Randall S, Crawford T, Currie J, River J, Betihavas V. Impact of community based nurse-led clinics on patient outcomes, patient satisfaction, patient access and cost effectiveness: A systematic review. Int J Nurs Stud. 2017; 73:24-33.
42. Hansen-Turton T, Sherman S, King ES. Nurse-led health clinics: operations, policy, and opportunities. 1 ed. New York: Springer Publishing Company; 2015. 273 p.
43. Hatchett R. Nurse-Led Clinics: Practical Issues. Psychology Press: Taylor & Francis; 2013. 119 p.
44. Ghisi GLdM, Abdallah F, Grace SL, Thomas S, Oh P. A systematic review of patient education in cardiac patients: Do they increase knowledge and promote health behavior change? Patient Educ Couns. 2014; 95(2):160-74.
45. Page T, Lockwood C, Conroy-Hiller T. Effectiveness of nurse-led cardiac clinics in adult patients with a diagnosis of coronary heart disease : systematic review. Int J Evid Based Healthc. 2005; 3(1):2-26.
46. Wormald R, Evans J. What Makes Systematic Reviews Systematic and Why are They the Highest Level of Evidence? Ophthalmic Epidemiol. 2018; 25(1):27-30.
47. Møller AM, Myles PS. What makes a good systematic review and meta-analysis? British journal of anaesthesia : BJA. 2016; 117(4):428-30.
48. Garritty C, Stevens A, Hamel C, Golfam M, Hutton B, Wolfe D. Knowledge Synthesis in Evidence-Based Medicine. Semin Nucl Med. 2019; 49(2):136-44.
49. Kendall JM. Designing a research project: randomised controlled trials and their principles. Emergency medicine journal : EMJ. 2003; 20(2):164-8.
50. Gopalakrishnan S, Ganeshkumar P. Systematic reviews and meta-analysis: Understanding the best evidence in primary healthcare. J Family Med Prim Care. 2013; 2(1):9-14.
51. Huang Y-J, Parry M, Zeng Y, Luo Y, Yang J, He G-P. Examination of a Nurse-led Community-based Education and Coaching Intervention for Coronary Heart Disease High-risk Individuals in China. Asian Nurs Res (Korean Soc Nurs Sci). 2017; 11(3):187-93.

52. Roth GA, Nguyen G, Forouzanfar MH, Mokdad AH, Naghavi M, Murray CJ. Estimates of global and regional premature cardiovascular mortality in 2025. Circulation. 2015; 132(13):1270-82.
53. Levitan EB, Muntner P, Chen L, Deng L, Kilgore ML, Becker D, et al. Burden of coronary heart disease rehospitalizations following acute myocardial infarction in older adults. Cardiovasc Drugs Ther. 2016; 30(3):323-31.
54. Dalen JE, Alpert JS, Goldberg RJ, Weinstein RS. The epidemic of the 20th century: coronary heart disease. Am J Med. 2014; 127(9):807-12.
55. Williamson D. Blood Circulatory System. OpenStax-CNX module, m43510. 2012.
56. Mackay J, Mensah GA. The atlas of heart disease and stroke. Centers for Disease Control and Prevention (U.S.): World Health Organization; 2004. 112 p.
57. Snaterse M, Dobber J, Jepma P, Peters RJ, Ter Riet G, Boekholdt SM, et al. Effective components of nurse-coordinated care to prevent recurrent coronary events: a systematic review and meta-analysis. Heart. 2016; 102(1):50-6.
58. Chiang C-Y, Choi K-C, Ho K-M, Yu S-F. Effectiveness of nurse-led patient-centered care behavioral risk modification on secondary prevention of coronary heart disease: A systematic review. Int J Nurs Stud. 2018; 84:28-39.
59. Koelewijn-van Loon MS, Van Der Weijden T, Van Steenkiste B, Ronda G, Winkens B, Severens JL, et al. Involving patients in cardiovascular risk management with nurse-led clinics: A cluster randomized controlled trial. CMAJ. 2009; 181(12):E267-E74.
60. de Melo Ghisi GL, Abdallah F, Grace SL, Thomas S, Oh P. A systematic review of patient education in cardiac patients: do they increase knowledge and promote health behavior change? Patient Educ Couns. 2014; 95(2):160-74.
61. National Heart Foundation of Australia. Reducing risk in heart disease: an expert guide to clinical practice for secondary prevention of coronary heart disease. National Heart Foundation of Australia Melbourne; 2012 [cited 2018 9 July]. Available from: https://www.heartfoundation.org.au/getmedia/a54598f9-e091-4637-b2be-aeed4244bf1e/Reducing-risk-in-heart-disease.pdf
62. Joanna Briggs Institute. The Joanna Briggs Institute Best Practice Information Sheet: Nurse-led interventions to reduce cardiac risk factors in adults. Nurs Health Sci. 2010; 12(3):288-91.
63. Wong FK, Chung LC. Establishing a definition for a nurse-led clinic: structure, process, and outcome. J Adv Nurs. 2006; 53(3):358-69.
64. Voogdt-Pruis HR, Vrijhoef HJ, Beusmans GH, Gorgels AP. Quality improvement of nurse-led aftercare to outpatients with coronary heart disease: report of a case study. Int J Qual Health Care. 2012; 24(3):286-92.
65. Schadewaldt V, Schultz T. Nurse-led clinics as an effective service for cardiac patients: Results from a systematic review. Int J Evid Based Healthc. 2011; 9(3):199-214.
66. Al-Mallah MH, Farah I, Al-Madani W, Bdeir B, Al Habib S, Bigelow ML, et al. The Impact of Nurse-Led Clinics on the Mortality and Morbidity of Patients with Cardiovascular Diseases: A Systematic Review and Meta-analysis. J Cardiovasc Nurs. 2016; 31(1):89-95.
67. Bethell H, Lewin R, Dalal H. Cardiac rehabilitation in the United Kingdom. Heart. 2009; 95(4):271-5.
68. Drozda J, Messer JV, Spertus J, Abramowitz B, Alexander K, Beam CT, et al. ACCF/AHA/AMA–PCPI 2011 performance measures for adults with coronary artery disease and hypertension: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Performance Measures and the American Medical Association–Physician Consortium for Performance Improvement. J Am Coll Cardiol. 2011; 58(3):316-36.

69. Lovibond SH, Lovibond PF. Manual for the depression anxiety stress scales. 2nd ed. ed. Sydney, N.S.W: Psychology Foundation of Australia; 1995. 41 p.
70. Joanna Briggs Institute. The System for the Unified Management, Assessment and Review of Information (SUMARI). [cited 2018 2 June]. Available from: https://sumari.jbi.global/
71. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med. 2009; 151(4):264-9.
72. Tufanaru C, Munn Z, Aromataris E, Campbell JL, Hopp L. Section 3: Systematic reviews of effectiveness. 2017 [cited 2020 20 December]. Available from: https://reviewersmanual.joannabriggs.org/
73. Cochrane Collaboration. Review manager (RevMan)[computer program]. Version; 2014 [cited Available from: https://training.cochrane.org/online-learning/core-software/revman
74. Scarborough P, Allender S, Rayner M, Goldacre M. An index of unhealthy lifestyle is associated with coronary heart disease mortality rates for small areas in England after adjustment for deprivation. Health & place. 2011; 17(2):691-5.
75. Joanna Briggs I. The Joanna Briggs Institute Best Practice Information Sheet: Nurse-led interventions to reduce cardiac risk factors in adults. Nursing & health sciences. 2010; 12(3):288-91.
76. Corones-Watkins K, Cooke M, Theobald K, White K, Thompson DR, Ski CF, et al. Effectiveness of nurse-led clinics in the early discharge period after percutaneous coronary intervention: A systematic review. Aust Crit Care. 2021; 34(5):510-7.
77. Debusk RF, Miller NH, Kraemer HC, Bandura A, Ghandour G, Clark M, et al. A case-management system for coronary risk factor modification after acute myocardial infarction. Ann Intern Med. 1994; 120(9):721-9.
78. Park M, Song R, Jeong J-O. Effect of goal attainment theory based education program on cardiovascular risks, behavioral modification, and quality of life among patients with first episode of acute myocardial infarction: Randomized study. International Journal of Nursing Studies. 2017; 71:8-16.
79. Zhang P, Hu Y-d, Xing F-M, Li C-Z, Lan W-F, Zhang X-L. Effects of a nurse-led transitional care program on clinical outcomes, health-related knowledge, physical and mental health status among Chinese patients with coronary artery disease: A randomized controlled trial. International Journal of Nursing Studies. 2017; 74:34-43.
80. Wood DA, Kotseva K, Connolly S, Jennings C, Mead A, Jones J, et al. Nurse-coordinated multidisciplinary, family-based cardiovascular disease prevention programme (EUROACTION) for patients with coronary heart disease and asymptomatic individuals at high risk of cardiovascular disease: a paired, cluster-randomised controlled trial. Lancet. 2008; 371(9629):1999-2012.
81. Saffi MA, Polanczyk CA, Rabelo-Silva ER. Lifestyle interventions reduce cardiovascular risk in patients with coronary artery disease: a randomized clinical trial. Eur J Cardiovasc Nurs. 2014; 13(5):436-43.
82. Woollard J, Burke V, Beilin LJ, Verheijden M, Bulsara MK. Effects of a General Practice-Based Intervention on Diet, Body Mass Index and Blood Lipids in Patients at Cardiovascular Risk. Eur J Prev Cardiol. 2003; 10(1):31-40.
83. Bartlett J, Predazzi IM, Williams SM, Bush WS, Kim Y, Havas S, et al. Is Isolated Low High-Density Lipoprotein Cholesterol a Cardiovascular Disease Risk Factor? New Insights From the Framingham Offspring Study. Circulation Cardiovascular quality and outcomes. 2016; 9(3):206-12.
84. Bianchi C, Penno G, Miccoli R, Del Prato S. Blood Glucose Control and Coronary Heart Disease. Herz. 2010; 35(3):148-59.

85. Legler S, Celano CM, Beale EE, Hoeppner BB, Huffman JC. Use of text messages to increase positive affect and promote physical activity in patients with heart disease: The Promoting Activity in Cardiac Patients via Text Messages (PACT) pilot study. Curr Psychol. 2020; 39(2):648-55.
86. Lahoud R, Chongthammakun V, Wu Y, Hawwa N, Brennan DM, Cho L. Comparing SF-36 ® scores versus biomarkers to predict mortality in primary cardiac prevention patients. Eur J Intern Med. 2017; 46:47-55.
87. Ware JE. SF-36 health survey update. Spine (Philadelphia, Pa 1976). 2000; 25(24):3130-9.
88. Burell G. Dangerous depression in cardiac patients: What can we do about it? Eur J Prev Cardiol. 2020; 27(5):473-7.
89. Sekhri N, Feder GS, Junghans C, Hemingway H, Timmis AD. How effective are rapid access chest pain clinics? Prognosis of incident angina and non-cardiac chest pain in 8762 consecutive patients. Heart (British Cardiac Society). 2007; 93(4):458-63.
90. Mourad G, Jaarsma T, Strömberg A, Svensson E, Johansson P. The associations between psychological distress and healthcare use in patients with non-cardiac chest pain: does a history of cardiac disease matter? BMC psychiatry. 2018; 18(1):172-.
91. Al-Maqbali M. Systematically assessing chest pain in cardiac patients. BJCN. 2014; 9(2):86-92.
92. Halcomb E, Moujalli S, Griffiths R, Davidson P. Effectiveness of general practice nurse interventions in cardiac risk factor reduction among adults. Int J Evid Based Healthc. 2007; 5(3):269-95.
93. Al-Ganmi AH, Perry L, Gholizadeh L, Alotaibi AM. Cardiovascular medication adherence among patients with cardiac disease: a systematic review. J Adv Nurs. 2016; 72(12):3001-14.
94. Ferdinand KC, Senatore FF, Clayton-Jeter H, Cryer DR, Lewin JC, Nasser SA, et al. Improving Medication Adherence in Cardiometabolic Disease: Practical and Regulatory Implications. J Am Coll Cardiol. 2017; 69(4):437-51.
95. Ceccarini M, Manzoni GM, Castelnuovo G. Assessing Depression in Cardiac Patients: What Measures Should Be Considered? Depress Res Treat. 2014; 2014(2014):148256-17.
96. Luo Z-C, Zhai L, Dai X. Does a Nurse-Led Program of Support and Lifestyle Management for patients with coronary artery disease significantly improve psychological outcomes among the patients?: A meta-analysis. Medicine (Baltimore). 2018; 97(35):e12171-e.
97. Connolly SB, Kotseva K, Jennings C, Atrey A, Jones J, Brown A, et al. Outcomes of an integrated community-based nurse-led cardiovascular disease prevention programme. Heart. 2017; 103(11):840-7.
98. Sutter RR, Cuellar AEAE, Harvey MM, Hong YAYA. Academic Nurse-Managed Community Clinics Transitioning to Telehealth: Case Report on the Rapid Response to COVID-19. JMIR nursing. 2020; 3(1):e24521-e.
99. Levy S, Henderson L, McAlpine C. Growing up with confidence: using telehealth to support continence self-care deficits amongst young people with complex needs. Inform Prim Care. 2014; 21(3):113-7.
100. Ling KKW. Effectiveness of an Advanced Practice Nurse-Led Telehealth on Readmissions and Health-Related Outcomes Among Patients Post Acute Myocardial Infarction: A Randomised Controlled Trial with Process Evaluation. ProQuest Dissertations Publishing; 2018. p. 426.
101. Moseley J, Carter-Templeton H, Aying J, Kristo G. Telehealth Utilization to Improve the General Surgery Patient Care Experience. J Nurse Pract. 2021; 17(8):958-62.
102. Tietjen KM, Breitenstein S. A Nurse-Led Telehealth Program to Improve Emotional Health in Individuals With Multiple Sclerosis. J Psychosoc Nurs Ment Health Serv. 2017; 55(3):31-7.

103. Whooley MA, de Jonge P, Vittinghoff E, Otte C, Moos R, Carney RM, et al. Depressive Symptoms, Health Behaviors, and Risk of Cardiovascular Events in Patients With Coronary Heart Disease. JAMA. 2008; 300(20):2379-88.
104. Zhou Y, Zhu X-P, Shi J-J, Yuan G-Z, Yao Z-A, Chu Y-G, et al. Coronary Heart Disease and Depression or Anxiety: A Bibliometric Analysis. Front Psychol. 2021; 12:669000-.
105. De Luca L, Temporelli PL, Amico AF, Gonzini L, Uguccioni M, Varani E, et al. Impact of history of depression on 1-year outcomes in patients with chronic coronary syndromes: An analysis of a contemporary, prospective, nationwide registry. Int J Cardiol. 2021; 331:273-80.
106. Calton B, Abedini N, Fratkin M. Telemedicine in the Time of Coronavirus. J Pain Symptom Manage. 2020; 60(1):e12-e4.
107. Royal Australian College of General Practitioners. Position Statement on Independent nurse-led clinics in primary healthcare. 2015 [cited 2021 9 August]. Available from: https://www.racgp.org.au/advocacy/position-statements/view-all-position-statements/health-systems-and-environmental/independent-nurse-led-clinics-in-primary-care#ref-num-23
108. Hudorovic N, Vicic-Hudorovic V. eComment. Nurse-led clinics and cost-effectiveness. Interact Cardiovasc Thorac Surg. 2012; 14(6):733-4.
109. Raftery JP, Yao GL, Murchie P, Campbell NC, Ritchie LD. Cost effectiveness of nurse led secondary prevention clinics for coronary heart disease in primary care: follow up of a randomised controlled trial. BMJ. 2005; 330(7493):707-10.
110. Driscoll A, Gao L, Watts JJ. Clinical effectiveness and cost-effectiveness of ambulatory heart failure nurse-led services: an integrated review. BMC Cardiovasc Disord. 2022; 22(1):64-.
111. Coleman S, Havas K, Ersham S, Stone C, Taylor B, Graham A, et al. Patient satisfaction with nurse-led chronic kidney disease clinics: A multicentre evaluation. Journal of renal care. 2017; 43(1):11-20.
112. Connolly C, Cotter P. Effectiveness of nurse-led clinics on healthcare delivery: An umbrella review. J Clin Nurs. 2021; 6(1):12-30.
113. Schober M, Lehwaldt D, Rogers M, Steinke M, Turale S, Pulcini J, et al. Guidelines on advanced practice nursing. 2020 [cited 2021 1 October]. Available from: https://www.icn.ch/system/files/documents/2020-04/ICN_APN%20Report_EN_WEB.pdf
114. Howe S. Nursing in Primary Health Care (NiPHC) Program – Enhanced Nurse Clinics: A review of Australian and international models of nurse clinics in primary health care settings 2016 [cited 2021 19 November]. Available from: https://www.apna.asn.au/docs/f221e342-13f3-e611-80d2-005056be66b1/Review%20of%20Australian%20and%20international%20models%20of%20nurse%20clinics.pdf
115. Hoare KJ, Mills J, Francis K. The role of Government policy in supporting nurse-led care in general practice in the United Kingdom, New Zealand and Australia: an adapted realist review. J Adv Nurs. 2012; 68(5):963-80.
116. Douglas C, Schmalkuche D, Nizette D, Yates P, Bonner A. Nurse-led services in Queensland: A scoping study. Collegian (Royal College of Nursing, Australia). 2018; 25(4):363-70.
117. Black JA, Cheng K, Flood JA, Hamilton G, Parker S, Enayati A, et al. Evaluating the benefits of a rapid access chest pain clinic in Australia. Med J Aust. 2019; 210(7):321-5.
118. Olivia C, Hastie C, Farshid A. Adherence to guidelines regarding anticoagulation and risk factors for progression of atrial fibrillation in a nurse-led clinic. Intern Med J. 2021; 51(7):1136-42.
119. Stewart S, Chan YK, Wong C, Jennings G, Scuffham P, Esterman A, et al. Impact of a nurse-led home and clinic-based secondary prevention programme to prevent progressive cardiac

dysfunction in high-risk individuals: the Nurse-led Intervention for Less Chronic Heart Failure (NIL-CHF) randomized controlled study. Eur J Heart Fail. 2015; 17(6):620-30.
120. Bush CT. Postgraduate Nurse Practitioner Training: What Nurse Executives Need to Know. J Nurs Adm. 2014; 44(12):625-7.
121. Middleton S, Gardner A, Della PR, Lam L, Allnutt N, Gardner G. How has the profile of Australian nurse practitioners changed over time? Collegian (Royal College of Nursing, Australia). 2016; 23(1):69-77.
122. Jackson D, Bradbury-Jones C, Baptiste D, Gelling L, Morin K, Neville S, et al. Life in the pandemic: Some reflections on nursing in the context of COVID-19. J Clin Nurs. 2020; 29(13-14):2041-3.
123. Fremming B, Ringenberg KJ, Schlawin B, Roberts EK, Schulte TE. Pandemic surgical classification is useful during nurse staffing shortages. J Clin Anesth. 2022; 79:110750-.
124. Halcomb E, McInnes S, Williams A, Ashley C, James S, Fernandez R, et al. The Experiences of Primary Healthcare Nurses During the COVID-19 Pandemic in Australia. J Nurs Scholarsh. 2020; 52(5):553-63.
125. Gilbert AW, Billany JCT, Adam R, Martin L, Tobin R, Bagdai S, et al. Rapid implementation of virtual clinics due to COVID-19: report and early evaluation of a quality improvement initiative. BMJ Open Quality. 2020; 9(2).
126. Nagata JM. Rapid Scale-Up of Telehealth During the COVID-19 Pandemic and Implications for Subspecialty Care in Rural Areas. The Journal of rural health. 2021; 37(1):145-.
127. Menotti A, Puddu PE. Can we still learn from the Seven Countries Study? Curr Opin Lipidol. 2018; 29(4):313-7.
128. Judd J. The practical issues of establishing paediatric orthopaedic nurse led clinics and judging success through parent satisfaction. J Orthop Nurs. 2009; 13(2):63-9.

Appendices

Appendix A

Search strategy

PubMed

Limitations:

Date: 1 January 2008 – February 2022

Language: English

Coronary heart disease	Nurse led clinics	Randomised Controlled Trial
"Coronary Disease"[mh:noexp] OR "coronary artery diseases"[mh] OR "coronary occlusion"[mh] OR "coronary stenosis"[mh] OR "coronary heart disease*"[tiab] OR "coronary disease*"[tiab] OR "myocardial infarction"[tiab] OR "coronary artery disease*"[tiab] OR "coronary occlusion"[tiab] OR cardiac[tiab]	"Practice Patterns, Nurses'"[mh] OR "nurse coordinated clinic*"[tiab] OR "nurse led clinic*"[tiab] OR "Nurse initiated"[tiab] OR "Nurse managed"[TIAB] OR "nurse led"[tiab]	"Clinical stud*"[all] OR "Randomised Controlled Trial*"[all] OR "Clinical trial*"[all] OR "Controlled Clinical Trial*"[all] OR "randomi*[all] OR "randomly"[all] OR "RCT*"[all]

	Search strategy dated 21.04.2019	Records retrieved
S1	"coronary disease"[mh:noexp]	130069
S2	"coronary artery diseases"[mh]	0
S3	"coronary stenosis"[mh]	17817
S4	"coronary heart disease*"[tiab]	48387
S5	"coronary disease*"[tiab]	19478
S6	"myocardial infarction"[tiab]	173225
S7	"coronary artery disease*"[tiab]	82933
S8	"coronary occlusion"[tiab]	6181
S9	cardiac[tiab]	580490
S10	"Practice Patterns, Nurses'"[mh]	2421
S11	"nurse coordinated clinic*"[tiab]	0
S12	"nurse led clinic*"[tiab]	171
S13	"Nurse initiated"[tiab]	323
S14	"Nurse managed"[tiab]	534
S15	"nurse led"[tiab]	3424
S16	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9	870981
S17	S10 OR S11 OR S 12 OR S13 OR S14 OR S15	2421
S18	"Randomised Controlled Trial*"[all]	512175
S19	"Clinical stud*"[all]	0
S20	"Clinical trial*"[all]	691680
S21	"Controlled Clinical Trial*"[all]	105967
S22	randomi*[all]	843161

S23	“randomly”[all]	317856
S24	“RCT*”[all]	20504
S25	S18 OR S 19 OR S20 OR S21 OR S22 OR S23 OR S 24	1417252
S26	S16 AND S17 AND S25	158

Appendix B

Rationale for Studies not included in the review

Study	Rationale for exclusion
Al-Ganmi AHA, Perry L, Gholizadeh L, Alotaibi AM. Behaviour change interventions to improve medication adherence in patients with cardiac disease: Protocol for a mixed methods study including a pilot randomised controlled trial. Collegian. 2018; 25(4):385-94.	Protocol
Assyag P, Boutron I, Boyer-Chatenet L, Dalichampt M, Steg PG, Montalescot G, et al. RESICARD prevention trial: A randomized multicentre study comparing standard care with supervised nurse-led therapeutic education. Results of a French network of cardiac risk-factor correction. European Heart Journal. 2011; 32:229.	Conference abstract
Bavry AA. Nurse-coordinated multidisciplinary, family-based cardiovascular disease prevention programme (EUROACTION). ACC Cardiosource Review Journal. 2008; 17(8):49-.	Same results as in Wood et al[15]
Brors G, Norekval TM, Skotnes LH, Fridlund B. The self-management behaviour after an individual nurse-led counselling programme for patients early discharged aftermyocardial infarction: A pilot randomised controlled trial. European Journal of Cardiovascular Nursing. 2016; 15:S100-S1.	Conference presentation
Buigues C, Queralt A, De Velasco JA, Salvador-Sanz A, Jennings C, Wood D, et al. Lipid Profile Results after Cardiovascular Prevention Programme: Euroaction Model in Spain. Endocr Metab Immune Disord Drug Targets. 2020; 20(9):1412-8	Spanish component of EUROACTION study
Chan Y, Carrington M, Calderone A, Stewart S. A randomised controlled study of a multidisciplinary, home-based health care program for privately insured cardiac patients: The Young @ Heart Study. Heart Lung and Circulation. 2010; 19:S243.	Secondary analysis of the studies
Chan Y-K, Stewart S, Calderone A, Scuffham P, Goldstein S, Carrington MJ, et al. Exploring the potential to remain "Young @ Heart": initial findings of a multi-centre, randomised study of nurse-led, home-based intervention in a hybrid health care system. International journal of cardiology. 2012; 154(1):52-8.	Secondary analysis of the studies
Chan SS, Leung DY, Lau C, Wong V, Lam T. Cost-effectiveness analysis of a low intensity nurse-led stage-matched smoking cessation intervention to cardiac patients in Hong Kong. Circulation. 2010;122(2):e87.	Conference presentation
Cohen A, Assyag P, Boyer-Chatenet L, Cohen-Solal A, Perdrix C, Dalichampt M, et al. An education program for risk factor management after an acute coronary syndrome a randomized clinical trial. JAMA Internal Medicine. 2014; 174(1):40-8.	Not an NLC
Corones-Watkins K, Theobald K, White K, Clark RA. A pilot study of a post-discharge nurse-led, educational intervention on cardiac selfefficacy and anxiety in post-PCI patients. Global Heart, 2014; 9(1):e336.	Conference presentation
Corones-Watkins K, Theobald K, White K. Self-management practices in post-PCI patients after attending a nurse-led clinic. Heart Lung and Circulation. 2016; 25:S302.	Conference presentation
Gaudel P, Neupane S, Koivisto A-M, Kaunonen M, Rantanen A. Effects of a lifestyle-related risk factor modification intervention on lifestyle changes among patients with coronary artery disease in Nepal. Patient Educ Couns. 2021; 104(6):1406-14.	Does not meet a PICO criteria

Study	Rationale for exclusion
Harald Thune Jorstad HT, Fagel ND, Scholte Op Reimer W, Tijssen JGP, Peter RJG. A nurse coordinated prevention program improves quality of life in coronary patients: Results from the RESPONSE trial. European Journal of Cardiovascular Prevention and Rehabilitation. 2011; 18(1):S2.	Conference abstract
Jiang W, Feng M, Gao C, Li J, Gao R, Wang W. Effect of a nurse-led individualized self-management program for Chinese patients with acute myocardial infarction undergoing percutaneous coronary intervention. Eur J Cardiovasc Nurs. 2020; 19(4):320-9.	Not RCT
Jorstad HT, Madelon Minneboo M, Fagel ND, Scholte Op Reimer WJ, Tijssen JG, Peters RJG. A nurse coordinated prevention program improves quality of life in coronary patients: Results from the response trial. European Journal of Preventive Cardiology. 2012; 19(1):S46.	Conference abstract
Jørstad HT, Alings AMW, Liem AH, Von Birgelen C, Tijssen JGP, De Vries CJ, et al. RESPONSE study: Randomised Evaluation of Secondary Prevention by Outpatient Nurse SpEcialists. Study design, objectives and expected results. Netherlands Heart Journal. 2009; 17(9):322-8.	Same results as Jorstad[8] 2013
Jorstad HT, Scholte Op Reimer WJ, Lenzen MJ, Tijssen JG, Peters RJG. Structuring a nurse led secondary prevention clinic: A multicenter experience in 700 patients. European Journal of Cardiovascular Nursing. 2010; 9:S27.	Same results as Jorstad[8] 2013
Jorstad HT, Von Birgelen C, Alings M, Liem A, Van Dantzig JM, Jaarsma W, et al. Improvement of risk factor control after an acute coronary syndrome by a nurse coordinated prevention program: Results from a randomized trial. Journal of the American College of Cardiology. 2011; 57(14):E549.	Conference abstract
Karataş T, Polat Ü. Effect of nurse-led program on the exercise behavior of coronary artery patients: Pender's Health Promotion Model. Patient Educ Couns. 2021; 104(5):1183-92	Includes rehabilitation programme
Koh KWL, Wang W, Richards AM, Chan MY, Cheng KKF. Effectiveness of advanced practice nurse-led telehealth on readmissions and health-related outcomes among patients with post-acute myocardial infarction: ALTRA Study Protocol. Journal of Advanced Nursing (John Wiley & Sons, Inc). 2016; 72(6):1357-67.	Protocol
Kure CE, Ski CF, Stewart S, Chan YK, Carrington MJ, Thompson DR. Potential impact of depression on health outcomes in a randomised control trial of multidisciplinary, nurse-led, home based intervention (HBI) to reduce secondary cardiac events. Global Heart. 2014; 9(1):e29.	Same results as Carrington et al[6] 2013
Lachman S, Minneboo M, Snaterse M, Jorstad HT, Ter Riet G, Scholte Op Reimer WJ, et al. Community-based comprehensive lifestyle programs in patients with coronary artery disease: Objectives, design and expected results of Randomized Evaluation of Secondary Prevention by Outpatient Nurse SpEcialists 2 trial (RESPONSE 2). American heart journal. 2015; 170(2):216-22.	Protocol
Lewis M, Chondros P, Mihalopoulos C, Lee YY, Gunn JM, Harvey C, et al. The assertive cardiac care trial: A randomised controlled trial of a coproduced assertive cardiac care intervention to reduce absolute cardiovascular disease risk in people with severe mental illness in the primary care setting. Contemp Clin Trials. 2020; 97:106143	Protocol
Lu CC, Hsiao YC, Huang HW, Lin JY, Huang CL. Effects of a Nurse-Led, Stage-Matched, Tailored Program for Smoking Cessation in Health Education Centers: A Prospective, Randomized, Controlled Trial. Clin Nurs Res. 2018:1054773817754276.	Authors did not reply to the request to provide data separately for CHD patients
Oranta O, Luutonen S, Salokangas RKR, Vahlberg T, Leino-Kilpi H. Nurse-led interpersonal counseling for depressive symptoms in patients with myocardial infarction. Cardiology (Switzerland). 2013	Abstract

Study	Rationale for exclusion
Pająk A, Wolfshaut-Wolak R, Doryńska A, Jankowski P, Fornal M, Grodzicki T, et al. Longitudinal effects of a nurse-managed comprehensive cardiovascular disease prevention program for hospitalized coronary heart disease patients and primary care high-risk patients. Kardiologia Polska (Polish Heart Journal). 2020; 78(5):429-37.	Polish component of EUROACTION study
Paoli G, Notarangelo MF, Mattioli M, La Sala R, Foà C, Solinas E, et al. ALLiance for sEcondary PREvention after an acute coronary syndrome. The ALLEPRE trial: A multicenter fully nurse-coordinated intensive intervention program. American Heart Journal. 2018; 203:12-6.	Protocol
Richards SH, Campbell JL, Dickens C, Anderson R, Gandhi M, Gibson A, et al. Enhanced psychological care in cardiac rehabilitation services for patients with new-onset depression: the CADENCE feasibility study and pilot RCT. Health Technol Assess. 2018; 22(30):1-220.	Rehabilitation
Rideout A, Lindsay G, Godwin J. Patient mortality in the 12 years following enrolment into a pre-surgical cardiac rehabilitation programme. Clinical Rehabilitation. 2012; 26(7):642-7.	Cardiac rehabilitation programme
Ruiz-Bustillo S, Ivern C, Badosa N, Farre N, Marco E, Bruguera J, et al. Efficacy of a nurse-led lipid-lowering secondary prevention intervention in patients hospitalized for ischemic heart disease: A pilot randomized controlled trial. Eur J Cardiovasc Nurs. 2019; 18(5):366-74.	Cardiac rehabilitation programme
Snaterse-Zuidam M, Heiligenberg M, Ter Riet G, Jorstad HT, Boekholdt SM, Scholte Op Reimer WJM, et al. Nurse-coordinated care improves risk reduction after acute coronary syndrome by stricter adherence to guideline recommended drug titration. European Heart Journal. 2016; 37:456.	Abstract
Stewart S, Carrington MJ, Goldstein S, Scuffham P. Differential impact of a nurse-led, home-based intervention for optimal secondary cardiac prevention on recurrent hospitalization in men and women: The Young @ Heart multicentre, randomized trial. European Heart Journal. 2013; 34:629.	Secondary analysis of the studies
Stewart S, Wiley JF, Ball J, Chan Y-K, Ahamed Y, Thompson DR, et al. Impact of Nurse-Led, Multidisciplinary Home-Based Intervention on Event-Free Survival Across the Spectrum of Chronic Heart Disease: Composite Analysis of Health Outcomes in 1226 Patients From 3 Randomized Trials. Circulation. 2016; 133(19):1867-77.	Secondary analysis of the studies
Verweij L, Jepma P, Buurman BM, Latour CHM, Engelbert RHH, Ter Riet G, et al. The cardiac care bridge program: design of a randomized trial of nurse-coordinated transitional care in older hospitalized cardiac patients at high risk of readmission and mortality. BMC Health Serv Res. 2018;18(1):508.	Not an NLC
Voogdt-Pruis H R, BeusmansGHM, Gorgels APM, van Ree JW. Nurse-led cardiovascular prevention is effective for both low-educated and higher-educated patients...PCNA's 16th Annual Poster Session at the Annual Symposium in Northwest Chicago, Illinois, April 15-17. Journal ofCardiovascular Nursing. 2010;25(5):364-5.	Abstract
Xueyu L, Shunlin X, Lijuan Z, Rongbin L, Jianrong W. Home-Based Exercise in Older Adults Recently Discharged From the Hospital for Cardiovascular Disease in China. Nursing Research. 2015; 64(4):246-55.	Cardiac rehabilitation programme
Yan Z, Jiali L, Fangming F, Mengting J, Chunyan Z, Xiaofang W. Effects of a Nurse-Led Phone Follow-up EducationProgram Based on the Self-efficacy Among Patients WithCardiovascular Disease. Journal of Cardiovascular Nursing. 2018; 33(1):E15-E23.	Does not meet populationn criteria
Zhang P, Xing F-M, Li C-Z, Wang F-L, Zhang X-L. Effects of a nurse-led transitional care programme on readmission, self-efficacy to implement health-promoting behaviours, functional status and life quality among Chinese patients with coronary artery disease: A randomised controlled trial. Journal of Clinical Nursing. 2018; 27(5-6):969-79.	Same trial as Zhang P, Hu Y-d, Xing F-M, Li C-Z, Lan W-F, Zhang X-L. Effects of a nurse-led transitional care program on clinical outcomes, health-related knowledge, physical and

Study	Rationale for exclusion
	mental health status among Chinese patients with coronary artery disease: A randomized controlled trial. International Journal of Nursing Studies. 2017; 74:34-43.
Zhao Y, Wong FKY. Effects of a post discharge transitional care programme for patients with coronary heart disease in China: A randomised controlled trial. Journal of Clinical Nursing. 2009; 18(17):2444-55.	Not an NLC

Included studies with missing data

Study	Missing data
Chan Y-K, Stewart S, Calderone A, Scuffham P, Goldstein S, Carrington MJ, et al. Exploring the potential to remain "Young @ Heart": initial findings of a multi-centre, randomised study of nurse-led, home-based intervention in a hybrid health care system. International journal of cardiology. 2012; 154(1):52-8.	Data was reported in %, rather than whole numbers. Authors did not respond.
Oranta O, Luutonen S, Salokangas RKR, Vahlberg T, Leino-Kilpi H. Depression-Focused Interpersonal Counseling and the Use of Healthcare Services After Myocardial Infarction. Perspect Psychiatr Care. 2012; 48(1):47-55.	Data is presented as graphs. Authors did not respond.
Oranta O, Luutonen S, Salokangas RK, Vahlberg T, Leino-Kilpi H. The outcomes of interpersonal counselling on depressive symptoms and distress after myocardial infarction. Nordic Journal of Psychiatry. 2010; 64(2):78-86.	Data is not presented as whole numbers. Authors did not respond.

Appendix C

Description of included studies

Authors	Year	Study	Design	Population	Setting	Description of intervention	Outcomes	Results
Barley EA, Walters P, Haddad M, Phillips R, Achilla E, McCrone P, et al. The UPBEAT nurse-delivered personalised care intervention for people with coronary heart disease who report current chest pain and depression: a randomised controlled pilot study. PLoS One. 2014; 9(6):e98704.	2014	UPBEAT	Randomised parallel group study.	Adults with symptomatic CHD (registered on GP CHD QOF register and reporting chest pain), reporting depression symptoms	Practices in South London	Personalised health plan for 6 months and followed for 1 year.	• Depression and anxiety • Chest pain • Quality of life • Cost-utility analysis	Trial and intervention procedures appeared to be feasible and acceptable. Personalised care allowed patients to work on unaddressed problems and appears cheaper than treatment as usual.
Carrington MJ, Chan YK, Calderone A, Scuffham PA, Esterman A, Goldstein S, et al. A multicenter, randomised trial of a nurse-led, home-based intervention for optimal secondary cardiac prevention suggests some benefits for men but not for women: the Young at Heart study. Circ Cardiovasc Qual Outcomes. 2013; 6(4):379-89.	2013	Young at Heart	Multi-centre randomised controlled trial	Adults > 18 years of age discharged to home with ay cardiac diagnosis requiring ongoing management	2 hospitals in Brisbane, Australia	Initial comprehensive home visit within 7-14 days post index hospitalisation, subsequent home visits, telephone coaching and referral to other health professionals and programmes.	• All-cause hospital stay • Cardiovascular admissions • All-cause mortality • Event-free survival	No difference in hospital activities between home-based intervention and usual care during 2 to 3 years follow-up.
Chan Y-K, Stewart S, Calderone A, Scuffham P, Goldstein S,	2012	Young at Heart	Multi-centre randomised	Adults > 18 years of age discharged to home with ay	2 hospitals in Brisbane, Australia	Initial comprehensive home visit within	• All-cause hospital stay during a mean	Early results demonstrate potential of long-term benefits

Authors	Year	Study	Design	Population	Setting	Description of intervention	Outcomes	Results
Carrington MJ, et al. Exploring the potential to remain "Young @ Heart": initial findings of a multi-centre, randomised study of nurse-led, home-based intervention in a hybrid health care system. International journal of cardiology. 2012; 154(1):52-8.			controlled trial	cardiac diagnosis requiring ongoing management		7-14 days post index hospitalisation, subsequent home visits, telephone coaching and referral to other health professionals and programmes.	of 2.5 years follow-up • All-cause and cardiovascular hospitalisation • Event-free survival • Healthcare costs	of home-based interventions for privately insured patients with chronic heart disease.
Corones-Watkins KM, Theobald KA, White KM. Outcomes of a randomised pilot trial of a nurse-led clinic for patients after percutaneous coronary intervention. Aust Crit Care. 2019; 32(4):285-92.	2019	Single study	Randomised pilot study.	Patients 18 and above who underwent PCI	Australian hospitals	Tailored education, health assessment, and post-discharge support with follow-up at Day 5-7 (Time 2), 1-month (Time 3), and 3-months (Time 4) post-hospital discharge	• Self-efficacy • Trait anxiety • Depression • Self-management	In Phase 1, intervention group participants did not show improvements in mental health indicators compared to standard care group participants, except for a moderate reduction in anxiety levels (d 1⁄4 0.50). Phase 2 qualitative findings highlighted the benefits of the nurse-led clinic.
Harold Jm Helmes HJM, Jorstad HT, Martens EJ, Van Dantzig JM, Tijssen JGP, Peters RJG. Effect of a nurse coordinated prevention program on levels of depression and anxiety in patients after an acute coronary syndrome: Results from	2011	RESPONSE	Prospective, randomised controlled trial	Patients (18-80 years) within 8 weeks after hospitalisation for an ACS	7 medical centres in The Netherlands	4 NCPP visits within the first 6 months after inclusion	• Health related quality of life • Depression	Statistically significant, albeit small decrease in depressive symptoms, especially in patients with moderate to severe depression

Authors	Year	Study	Design	Population	Setting	Description of intervention	Outcomes	Results
the RESPONSE trial. European Journal of Cardiovascular Prevention and Rehabilitation. 2011; 18(1): S44.								
Jorstad HT, Von Birgelen C, Alings AMW, Liem A, Van Dantzig JM, Jaarsma W, et al. Effect of a nurse-coordinated prevention programme on cardiovascular risk after an acute coronary syndrome: Main results of the RESPONSE randomised trial. Heart. 2013; 99(19):1421-30.	2013	RESPONSE	Prospective, randomised clinical trial	Patients (18-80 years) within 8 weeks after hospitalisation for an ACS	11 hospitals in the Netherlands	4 outpatient clinic visits to a cardiovascular nurse during the first 6 months at weeks 2, 7, 12 and 17 after baseline	• Risk factors • Hospital readmission in 12 months	Nurse-coordinated prevention programme with up to four outpatient clinic visits resulted in sustained lowering of cardiovascular risk in patients with coronary disease.
Jørstad HT, Minneboo M, Helmes HJM, Fagel ND, Scholte op Reimer WJ, Tijssen JGP, et al. Effects of a nurse-coordinated prevention programme on health-related quality of life and depression in patients with an acute coronary syndrome: results from the RESPONSE randomised controlled trial. BMC Cardiovascular Disorders. 2016; 16:1-9.	2016	REPONSE	Randomised control trial	Patients 18–80 years of age, admitted for ACS (ST-segment myocardial infarction, non-ST-segment elevation myocardial infarction or unstable angina pectoris)	11 hospitals in the Netherlands from June 2006 to July 2009	4 outpatient clinic visits to a cardiovascular nurse during the first 6 months	• Risk factors • Framingham Coronary Risk Score • Cumulative numbers of hospital readmission in 12 months	Significant improvement in HRQOL in patients with an ACS. Improvement was seen across the emotional, physical and social dimensions of HRQOL. NCPP was found to reduce depressive symptoms in patients.
Oranta O, Luutonen S, Salokangas RK, Vahlberg T, Leino-Kilpi H.	2011	Single study	Randomised control trial	Patients < 75 years old with the	University hospital in Finland	Interpersonal counselling from 1 to 6 sessions	• Health-related quality of life	IPC had positive effects of HRQOL in patient under 60

Authors	Year	Study	Design	Population	Setting	Description of intervention	Outcomes	Results
The effects of interpersonal counselling on health-related quality of life after myocardial infarction. J Clin Nurs. 2011; 20(23-24):3373-82.				diagnosis of acute MI		consisting of a starting (sessions 1-2), encouragement First session in hospital, the rest – by phone.		years. The improvement was significant in the intervention group.
Oranta O, Luutonen S, Salokangas RKR, Vahlberg T, Leino-Kilpi H. Depression-Focused Interpersonal Counseling and the Use of Healthcare Services After Myocardial Infarction. Perspect Psychiatr Care. 2012; 48(1):47-55.	2012	Single study	Randomised control trial	Patients < 75 years old with the diagnosis of acute MI	University hospital in Finland	Interpersonal counselling from 1 to 6 sessions consisting of a starting (sessions 1-2), encouragement First session in hospital, the rest – by phone.	• The use of healthcare services during 6 and 18 months after hospital discharge • Association between patient characteristics and the use of healthcare services	IPC seem to have some effects that decrease the use of healthcare services after MI.
Oranta O, Luutonen S, Salokangas RK, Vahlberg T, Leino-Kilpi H. The outcomes of interpersonal counselling on depressive symptoms and distress after myocardial infarction. Nordic Journal of Psychiatry. 2010; 64(2):78-86.	2010	Single study	Randomised control trial	Patients < 75 years old with the diagnosis of acute MI	University hospital in Finland	Interpersonal counselling from 1 to 6 sessions consisting of a starting (sessions 1-2), encouragement First session in hospital, the rest – by phone.	• Depressive symptoms and distress during 18 months of follow-up	IPC seem to reduce depressive symptoms and distress after MI.
Park M, Song R, Jeong J-O. Effect of goal attainment theory based education program on cardiovascular risks,	2017	Single study	Randomised controlled trial	Patients diagnosed with a first episode of AMI (ST-elevation MI, non-ST-elevation MI),	Cardiovascular centre of a university hospital, South Korea	The goal-attainment-based education program was designed to set the mutually	• Cardiovascular disease risks • Cardiac health behaviour scale • Quality of life	The participants who received the education program showed significantly better blood glucose

Authors	Year	Study	Design	Population	Setting	Description of intervention	Outcomes	Results
behavioral modification, and quality of life among patients with first episode of acute myocardial infarction: Randomized study. International Journal of Nursing Studies. 2017; 71:8-17.				admitted to the cardiac units for 3days or longer for percutaneous coronary intervention.		agreed goals of risk management and the behavioural modification strategies for achieving those goals.		control than those in the usual care group. The individuals who received the goal-oriented education showed significantly better health behaviours and quality of life compared to those who received usual care only.
Saffi MA, Polanczyk CA, Rabelo-Silva ER. Lifestyle interventions reduce cardiovascular risk in patients with coronary artery disease: a randomised clinical trial. Eur J Cardiovasc Nurs. 2014; 13(5):436-43.	2014	Single study	Randomised controlled trial	Patients age≥18 years, diagnosis by catheterization, treatment of acute coronary syndrome	Teaching hospital in Southern Brazil	Nurse-led guidance by means of five face-to-face sessions and telephone contact over the course of one year, starting three months after hospital discharge. Exercise and dietary goals were set for each patient and monitored at each session.	• 10-year cardiovascular risk (Framingham Risk Score) • Improvement in laboratory (lipid profile, blood glucose, etc. • Adherence to pharmacological treatment	One-year-long program of systematic nurse- led lifestyle counselling reduced cardiovascular risk scores, estimated effects over 10 years, by 1.7 points in a sample of CAD patients. There was significant improvement in secondary outcomes such as weight and systolic and diastolic blood pressure.
Smith PM, Burgess E. Smoking cessation initiated during hospital stay for patients with coronary artery disease: A	2009	Single study	Randomised control trial	Patients 18 years of age or older admitted because of acute MI or for CABG	Large urban hospital in Western Canada	Intervention included the minimal intervention plus 60 minutes of bedside counselling, take-	• Smoking status at 3, 6 and 12 months	More patients in the intensive intervention than in the minimal intervention were abstinent at 1 year. The odds of quitting smoking were 2 times

Authors	Year	Study	Design	Population	Setting	Description of intervention	Outcomes	Results
randomized controlled trial. Canadian Medical Association Journal. 2009; 180(13):1297-303.						home materials and 7 nurse-initiated counselling calls for 2 months after discharge.		greater for those in the intensive intervention.
Snaterse M, Jorstad HT, Heiligenberg M, Ter Riet G, Boekholdt SM, Scholte Op Reimer W, et al. Nurse-coordinated care improves the achievement of LDL cholesterol targets through more intensive medication titration. Open Heart. 2017; 4(2):e000607.	2017	RESPONCE	Randomised control trial	Patients aged 18–80 years were eligible if they had been diagnosed with ACS within 8 weeks prior to entry into the trial.	11 centres in the Netherlands	Patients visited the outpatient clinic up to four times during the first 6 months after inclusion, in addition to outpatient clinic visits to their cardiologist (usual care).	• Lipid-lowering medication titration	NCC resulted in more intensive medication titration among patients hospitalised for ACS, compared with usual care alone. A higher proportion of patients in the NCC group were on target compared with the usual care group.
Wood DA, Kotseva K, Connolly S, Jennings C, Mead A, Jones J, et al. Nurse-coordinated multidisciplinary, family-based cardiovascular disease prevention programme (EUROACTION) for patients with coronary heart disease and asymptomatic individuals at high risk of cardiovascular disease: a paired, cluster-randomised controlled	2008	EUROACTION	Cluster randomised controlled trial	Patients with coronary heart disease in hospitals and at high risk patients of developing cardiovascular disease	12 (six pairs) general hospitals in France, Italy, Poland, Spain, Sweden, and the UK, and 12 (six pairs) general-practice centres in Denmark, Italy, Poland, Spain, the Netherlands, and the UK.	Preventive cardiology intervention programme in hospital and general practice (eight sessions—one every week)	• Family-based lifestyle change • Management of blood-pressure, lipids and blood glucose • Prescription of cardioprotective drugs	Program reduced the risk of cardiovascular disease compared with usual care Blood pressure control was improved and for patients with coronary heart disease without the use of additional antihypertensive drugs. Control of blood cholesterol concentrations in these patients was improved in both the intervention and usual-care groups;

Authors	Year	Study	Design	Population	Setting	Description of intervention	Outcomes	Results
trial. Lancet. 2008; 371(9629):1999-2012.								
Zhang P, Hu Y-d, Xing F-M, Li C-Z, Lan W-F, Zhang X-L. Effects of a nurse-led transitional care program on clinical outcomes, health-related knowledge, physical and mental health status among Chinese patients with coronary artery disease: A randomized controlled trial. International Journal of Nursing Studies. 2017; 74:34-43.	2017	Single study	Randomised controlled trial	Patients with angina or myocardial infarction	Top level general hospital located in the centre of Tang Shan, a northern city in mainland China	Nurse-led transitional care intervention included a structured assessment and health education, followed by 7 months of individual teaching and coaching (home visits, telephone follow-up and group activity)	• Cardiovascular risk factors • Knowledge of CAD • Physical and mental health status	Majority of the clinical outcomes showed significant differences between the control and intervention groups over time. Nurse-led transitional care program could improve the physical and mental health status of CAD patients.

Description of studies from 2010 review[2]

Authors	Year	Study	Design	Population	Setting	Description of intervention	Outcomes	Results
Campbell NC, Ritchie LD, Thain J, Deans HG, Rawles JM, Squair JL. Secondary prevention in coronary heart disease: a randomised trial of nurse	1998	Single study	Randomised controlled trial	Patients (<80 years) with a working diagnosis of CHD, but without dementia or terminal illness	General practices in northeast Scotland, rural and urban areas	Nurses promoted medical and lifestyle aspects of secondary prevention and offered regular	Aspirin management, Blood pressure and lipid management,	Nurse ed c n cs n pr mary care can mprove both med ca and festy e components of

Authors	Year	Study	Design	Population	Setting	Description of intervention	Outcomes	Results
led clinics in primary care. Heart (British Cardiac Society). 1998; 80(5):447-52.				and not housebound.		follow up. Patients were invited for a first appointment during the first three months and were followed up depending on clinical circumstances (usually 2 to 6 month).	Dietary habits, physical activity, Smoking status, BMI, Health status (SF36), Angina symptoms, Anxiety and depression, Readmission rates Total mortality	secondary prevent on effect ve y.
Campbell NC, Thain J, Deans HG, Ritchie LD, Rawles JM, Squair JL. Secondary prevention in coronary heart disease: baseline survey of provision in general practice. 1998; 316:1430–4.	1998	Single study	Randomised controlled trial	Patients (<80 years) with a working diagnosis of CHD, but without dementia or terminal illness and not housebound.	General practices in northeast Scotland, rural and urban areas	Nurses promoted medical and lifestyle aspects of secondary prevention and offered regular follow up. Patients were invited for a first appointment during the first three months and were followed up depending on clinical circumstances (usually 2 to 6 month).	Aspirin management, Blood pressure and lipid management, Dietary habits, physical activity, Smoking status, BMI, Health status (SF36), Angina symptoms, Anxiety and depression, Readmission rates Total mortality	More than 90% of pat ents had rece ved b ood pressures checks w th n the past three years and more than 90% of these were managed n accordance w th gu de nes. L p d management was arge y neg ected, desp te the ex stence of oca gu de nes.
Delaney EK, Murchie P, Lee AJ, Ritchie LD, Campbell NC. Secondary prevention clinics for coronary heart disease: a	2008	Single study	Randomised controlled trial	Patients (<80 years) with a working diagnosis of CHD, but without dementia or terminal illness	General practices in northeast Scotland,	Nurses promoted medical and lifestyle aspects of secondary prevention and	Aspirin management, Blood pressure and lipid management,	There were no significant differences in the distribution of causes of death between

Authors	Year	Study	Design	Population	Setting	Description of intervention	Outcomes	Results
10-year follow-up of a randomised controlled trial in primary care. Heart. 2008; 94(11):1419-23.				and not housebound.	rural and urban areas	offered regular follow up. Patients were invited for a first appointment during the first three months and were followed up depending on clinical circumstances (usually 2 to 6 month).	Dietary habits, physical activity, Smoking status, BMI, Health status (SF36), Angina symptoms, Anxiety and depression, Readmission rates Total mortality	groups at either the 4- or 10-year follow-up. There was also no significant difference in the total number of hospital admissions between the two groups.
Murchie P, Campbell NC, Ritchie LD, Simpson JA, Thain J. Secondary prevention clinics for coronary heart disease: four year follow up of a randomised controlled trial in primary care. BMJ (Clinical research ed). 2003; 326(7380):84.	2003	Single study	Randomised controlled trial	Patients (<80 years) with a working diagnosis of CHD, but without dementia or terminal illness and not housebound.	General practices in northeast Scotland, rural and urban areas	Nurses promoted medical and lifestyle aspects of secondary prevention and offered regular follow up. Patients were invited for a first appointment during the first three months and were followed up depending on clinical circumstances (usually 2 to 6 month).	Aspirin management, Blood pressure and lipid management, Dietary habits, physical activity, Smoking status, BMI, Health status (SF36), Angina symptoms, Anxiety and depression, Readmission rates Total mortality	S gn f cant mprovements were shown n the ntervent on group n a components of secondary prevent on except smok ng at one year, and these were susta ned after four years except for exerc se.
Murchie P, Campbell N, Ritchie L, Deans H, Thain J. Effects of secondary prevention clinics on health status in patients	2004	Single study	Randomised controlled trial	Patients (<80 years) with a working diagnosis of CHD, but without dementia or terminal illness	General practices in northeast Scotland,	Nurses promoted medical and lifestyle aspects of secondary prevention and	Aspirin management, Blood pressure and lipid management,	At 1 year, there were significant improvements in five of eight SF-36 domains (all

Authors	Year	Study	Design	Population	Setting	Description of intervention	Outcomes	Results
with coronary heart disease: 4 year follow-up of a randomized trial in primary care. Fam Pract. 2004; 21(5):567-74.				and not housebound.	rural and urban areas	offered regular follow up. Patients were invited for a first appointment during the first three months and were followed up depending on clinical circumstances (usually 2 to 6 month).	Dietary habits, physical activity, Smoking status, BMI, Health status (SF36), Angina symptoms, Anxiety and depression, Readmission rates Total mortality	functioning scales, pain and general health) in the intervention group. No significant effects were observed on anxiety or depression at 1 or 4 years.
Jiang X, Sit JW, Wong TK. A nurse-led cardiac rehabilitation programme improves health behaviours and cardiac physiological risk parameters: evidence from Chengdu, China. J Clin Nurs. 2007; 16(10):1886-97.	2007	Single study	Randomised controlled trial	Pat ents f rst hosp ta sed w th AP or MI, v ng at home after d scharge.	2 tert ary med ca centres n Chengdu, south-west Ch na	12-week nurse-led programme, hospital- initiated, continued at home. Phase I at hospital: Individual health education lessons for patient and family members on self-management treatment, medical management, prevention and management, physical exercise, dietary management, smoking cessation, family support; and provision of a healthy heart manual Phase II at home: follow-up through	Smok ng cessat on, Wa k ng performance, D et and med cat on adherence	The resu ts of th s study nd cate the benef ts of a nurse- ed card ac rehab tat on ntervent on on hea th behav our mprovement and card ac phys o og ca r sk reduct on of CHD pat ents.

Authors	Year	Study	Design	Population	Setting	Description of intervention	Outcomes	Results
						home visits + phone-calls.		
Jolly K, Bradley F, Sharp S, Smith H, Thompson S, Kinmonth A-L, et al. Randomised controlled trial of follow up care in general practice of patients with myocardial infarction and angina: final results of the Southampton heart integrated care project. 1999; 318:706–11.	1999	Single study	Randomised controlled trial	Pat ents adm tted hosp ta w th AP or MI	Genera pract ces n Southampton and Southwest Hampsh re, Eng and	Structured fo ow-up care. Pract ce nurses (PN) n the ntervent on pract ces attended a tra n ng course on behav our change mode s and promot on of therapy adherences. Loca gu de nes for the care of CHD pat ents were deve oped and handed out to the ntervent on pract ces.	B ood pressure, Cho estero , Smok ng cessat on, Phys ca act v ty, BMI, Anx ety and depress on, Ang na symptoms, Qua ty of fe, Drug treatment, Pract ce attendance	Benefits for diet and exercise were small and did not reach statistical significance. Low attendance at the cardiac rehabilitation programme by 4 months.
Jolly K, Bradley F, Sharp S, Smith H, Mant D. Follow-up care in general practice of patients with myocardial infarction or angina pectoris: initial results of the SHIP trial. Fam Pract. 1998; 15(6):548-55.	1998	Single study	Randomised controlled trial	Pat ents adm tted hosp ta w th AP or MI	Genera pract ces n Southampton and Southwest Hampsh re, Eng and	Structured fo ow-up care. Pract ce nurses (PN) n the ntervent on pract ces attended a tra n ng course on behav our change mode s and promot on of therapy adherences. Loca gu de nes for the care of CHD pat ents were deve oped and handed out to the ntervent on pract ces	B ood pressure, Cho estero , Smok ng cessat on, Phys ca act v ty, BMI, Anx ety and depress on, Ang na symptoms, Qua ty of fe, Drug treatment, Pract ce attendance	The programme d d not mprove object ve measures of r sk. The emphas s of the educat ona programme for nurses n genera pract ce and rehab tat on, wh ch h gh ghted the mportance of mot vat ng behav our change and the ke hood of fu recovery after myocard a nfarct on, was at odds w th pat ents' exper ences
Khunti K, Stone M, Paul S, Baines J, Gisborne L, Farooqi A, et al. Disease management programme for secondary prevention of coronary heart disease and heart failure in primary	2007	Single study	Randomised controlled trial	Patients with CHD or CHF, CHD cohort of 1080 patients, only data of CHD patients used	All primary care practices of Leicester, UK	Patient assessment, confirmation of diagnosis by investigations, medication management and	Health status (SF36), Angina symptoms, Appropriate assessment,	A nurse-led disease management programme in primary care can lead to improvement in quality of care, including secondary

Authors	Year	Study	Design	Population	Setting	Description of intervention	Outcomes	Results
care: a cluster randomised controlled trial. 2007.						titration, home visits for house-bound patients with CHF and liaison between primary and secondary care.	Achievement of certain target levels, Blood pressure, Cholesterol, BMI Follow-up: 12 months	prevention, for patients with CHD and CHF.
Lapointe F, Lepage S, Larrivée L, Maheux P. Surveillance and treatment of dyslipidemia in the post-infarct patient: Can a nurse-led management approach make a difference? Can J Cardiol. 2006; 22(9):761-7.	2006	Single study	Randomised controlled trial	Pat ents d scharged from hosp ta after d agnosed pr mary MI, (<70 years)	Major acute care hosp ta and nearby genera pract ces n Sherbrooke, Quebec, Canada	Phone ca by a nurse after d scharge of hosp ta for educat ona messages on r sk management and treatment of r sk factors, emphas s ng the mportance of fo ow-up for p d eve s.	Hea th status (SF36), Comp ance n med cat on ntake, T me spent w th nurse, B ood p ds	No benefit in terms of lipids, quality of life or longer-term adherence to lipid-lowering medications up to 18 months after the hospitalization for an MI were demonstrated.
McHugh F, Lindsay GM, Hanlon P, Hutton I, Brown MR, Morrison C, et al. Nurse led shared care for patients on the waiting list for coronary artery bypass surgery: a randomised controlled trial. Heart (British Cardiac Society). 2001; 86(3):317-23.	2001	Single study	Randomised controlled trial	Pat ents wa t ng for CABG	Genera pract ces n G asgow, UK	Month y hea th educat on sess ons a ternate y n the pat ents home by a spec a st card ac a son nurse and n the genera pract ce he d by a nurse of the GP team. Informat on was ta ored to the pat ent s needs and the r w ngness to change behav our.	Smok ng status, BMI, Phys ca act v ty, b ood pressure, cho estero , ach evement of certa n target eve s, hea th status (SF 36), anx ety and depress on, pat ent sat sfact on;	Intervent on group was more ke y to stop smok ng and reduce obes ty. Target b ood pressure mproved n the contro group. However, there was no s gn f cant d fference between groups w th cho estero concentrat ons. There was a s gn f cant mprovement n genera hea th status scores across a e ght doma ns of the 36- tem short form hea th survey. Leve s of

Authors	Year	Study	Design	Population	Setting	Description of intervention	Outcomes	Results
								anx ety and depress on mproved.
Woollard J, Burke V, Lj B. Effects of general practice-based nurse-counselling on ambulatory blood pressure and antihypertensive drug prescription in patients at increased risk of cardiovascular disease. J Hum Hypertens. 2003; 17(10):689.	2003	Single study	Randomised controlled trial	20-75 years o d, d agnosed w th hypertens on, Type II D abetes or CHD Data on y from CHD pat ents used.	Pr mary care pract ces n Perth, Austra a	Programme on festy e changes, nc ud ng we ght reduct on, ncreased phys ca act v ty, encouragement n smok ng cessat on and d et adv ce, g ven by two nurses, tra ned n counse ng techn ques.	B ood pressure, heart rate, B ood p ds, BMI D etary ntake, drug treatment	After 18 months, targets for BP contro were not met n about 60% of pat ents and a most 50% had c n c BP above 140/ 90 mmHg. Year- ong nteract on w th nurse-counse ors may nf uence onger-term ant hypertens ve drug prescr pt on, poss b y by mprov ng comp ance. Subopt ma BP contro suggests that cont nu ng phys c an educat on on BP targets s needed.
Woollard J, Burke V, Beilin LJ, Verheijden M, Bulsara MK. Effects of a General Practice-Based Intervention on Diet, Body Mass Index and Blood Lipids in Patients at Cardiovascular Risk. European Journal of Preventive Cardiology. 2003; 10(1):31-40.	2003	Single study	Randomised controlled trial	20-75 years o d, d agnosed w th hypertens on, Type II D abetes or CHD Data on y from CHD pat ents used.	Pr mary care pract ces n Perth, Austra a	Programme on festy e changes, nc ud ng we ght reduct on, ncreased phys ca act v ty, encouragement n smok ng cessat on and d et adv ce, g ven by two nurses, tra ned n counse ng techn ques.	B ood pressure, heart rate, B ood p ds, BMI D etary ntake, drug treatment	Improved dietary habits and more favourable lipid profile were demonstrated. No clear benefits were seen on blood lipids, diet or body mass from participation in an intensive programme

Appendix D

Critical Appraisal

1. Critical appraisal results for included studies using the JBI-Critical Appraisal Checklist for randomised controlled trials

	Barley et al 2014	Carrington et al 2014	Chan et al 2012	Corones-Watkins et al 2019	Jiang et al 2020	Jorstad et al 2016	Jorstad et al 2013	Karatas et al 2020	Oranta et al 2011	Oranta et al 2012	Oranta et al 2010	Park et al 2017	Saffi et al 2014	Smith et al 2009	Wood et al 2008	Zhang et al 2017
1. True random zat on used for ass gnment of part c pants to treatment groups	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unc ear	Unc ear	Unc ear	Yes	Yes	Yes	Unc e ar	Yes
2. A ocat on concea ment	Yes	Unc ear	Unc ear	Yes	Yes	Unc ear	Unc ear	Yes	Unc ear	Unc ear	Unc ear	Yes	Unc e ar	Unc ear	Unc e ar	Yes
3. S m ar ty of treatment groups at the base ne	Yes	Yes	Yes	No	Yes	Yes/Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unc e ar	Yes
4. B nd ng of part c pants to treatment ass gnment	No	Yes	No	Yes	No	Unc ear	Yes	Unc ear	No	No	No	No	No	No	No	Yes
5. B nd ng of those de ver ng treatment	No	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No	No	No
6. B nd ng of outcomes assessment	Yes	Yes	Yes	No	Yes	Unc ear	Yes	Unc ear	Unc ear	Unc ear	Unc ear	Unc ear	Unc e ar	Unc ear	Unc e ar	Yes
7. Treatment groups treated dent ca y other than the ntervent on of nterest	Yes	Yes	Yes	No	Unc ear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Unc e ar	Yes
8. Fo ow up comp et on	No	Yes	Unc ear	No	Unc ear	No	Yes	Yes	No	No	No	Yes	Yes	Yes	No	Yes
9. Part c pants ana ys s n the	Yes	No	Yes	Yes	No	No	No	No	No	No	No	No	Yes	Yes	Yes	Yes

	Barley et al 2014	Carrington et al 2014	Chan et al 2012	Corones-Watkins et al 2019	Jiang et al 2020	Jorstad et al 2016	Jorstad et al 2013	Karatas et al 2020	Oranta et al 2011	Oranta et al 2012	Oranta et al 2010	Park et al 2017	Saffi et al 2014	Smith et al 2009	Wood et al 2008	Zhang et al 2017
groups to wh ch they were random sed																
10. Outcomes measurement n the same way for treatment groups	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
11. Outcomes measurement re ab ty	Unc ear	Unc ear	Unc ear	No	Unc ear	Unc ear	Unc ear	Unc ear	Unc ear	Unc ear	Unc ear	Unc ear	Yes	Yes	Yes	Yes
12. Appropr ate stat st ca ana ys s	Yes	Yes	N/A	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
13. Appropr ate tr a des gn, and any dev at ons from the standard RCT des gn	Yes	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No

2. Critical appraisal results for studies from the previous review using the JBI-Critical Appraisal Checklist for randomised controlled trials

	Campbell, Ritchie et al, 1998	Campbell, Thain et al, 1998	Delaney et al, 2008	Murchie et al, 2004	Murchie et al, 2003	Jiang et al, 2007	Khunti et al, 2007	Lapointe et al, 2006	McHugh et al, 2001	Jolly et al, 1999	Jolly et al, 1998	Woollard et al, 2003 JCR	Woollard et al, 2003 JHH
1. True randomization used for assignment of participants to treatment groups	Yes	Yes	Yes	Yes	Yes	yes	No	No	Unclear	Yes	Yes	Yes	Yes
2. Allocation concealment	Unclear	Unclear	Unclear	Unclear	Unclear	unclear	unclear	unclear	unclear	Unclear	Unclear	Yes	Yes
3. Similarity of treatment groups at the baseline	Unclear	Yes	Yes	Yes	Yes	yes	No	yes	yes	Yes	No	Yes	Yes
4. Blinding of participants to treatment assignment	No	No	No	No	No	unclear	unclear	no	unclear	No	No	No	No
5. Blinding of those delivering treatment	No	No	No	No	No	no	no	no	no	No	No	No	No
6. Blinding of outcomes assessment	Unclear	No	Unclear	Yes	Unclear	yes	unclear	unclear	no	Unclear	Unclear	No	No

	Campbell, Ritchie et al, 1998	Campbell, Thain et al, 1998	Delaney et al, 2008	Murchie et al, 2004	Murchie et al, 2003	Jiang et al, 2007	Khunti et al, 2007	Lapointe et al, 2006	McHugh et al, 2001	Jolly et al, 1999	Jolly et al, 1998	Woollard et al, 2003 JCR	Woollard et al, 2003 JHH
7. Treatment groups treated identically other than the intervention of interest	Yes	Yes	Yes	Yes	Yes	yes	Yes	No	yes	Unclear	Unclear	Yes	Yes
8. Follow up completion	Yes	Yes	Yes	Yes	Yes	No	yes	no	No	Yes	Yes	Yes	Yes
9. Participants analysis in the groups to which they were randomised (ITT)	Yes	Yes	Yes	Yes	Yes	yes	yes	no	no	Yes	Yes	Yes	Yes
10. Outcomes measurement in the same way for treatment groups	Yes	Yes	Yes	Yes	Yes	yes	yes	yes	yes	Yes	Yes	Yes	Yes
11. Outcomes measurement reliability	No	Yes	Yes	Yes	No	unclear	yes	unclear	No	Yes	Yes	Yes	Yes
12. Appropriate	Yes	Yes	Yes	Yes	Yes	yes	yes	yes	yes	Yes	Yes	Yes	Yes

	Campbell, Ritchie et al, 1998	Campbell, Thain et al, 1998	Delaney et al, 2008	Murchie et al, 2004	Murchie et al, 2003	Jiang et al, 2007	Khunti et al, 2007	Lapointe et al, 2006	McHugh et al, 2001	Jolly et al, 1999	Jolly et al, 1998	Woollard et al, 2003 JCR	Woollard et al, 2003 JHH
statistical analysis													
13. Appropriate trial design, and any deviations from the standard RCT design	Yes	Yes	No	No	No	yes	yes	yes	yes	Yes	Yes	Yes	Yes

Appendix E

Tables

Table 1 Results on all-cause mortality (4-year follow-up) from a study not included in meta-analysis

ST – short-term, MT- medium-term, LT – long-term

Outcome Type	Outcome subtype	Time frame	Study	Intervention	Control	Odd Ratio (95% CI)	P value
All-cause mortality	Mortality	LT - 4 years follow-up	Delaney et al. 2007	100/673	125/670	0.76 (0.57-1.01)	0.06

Table 2 Results on chest pain from studies not included in meta-analysis

Outcome type	Outcome subtype	Time frame	Study	Intervention	Control	Odd Ratio (95% CI)	P value
Symptoms	Chest pain and angina	ST	Barley et al. 2014	27/41	29/40	0.73 (0.28-1.89)	0.52
Symptoms	Chest pain and angina	MT	Barley et al. 2014	22/35	32/39	0.37 (0.13-1.08)	0.07

Table 3 Results on blood lipids from studies were not included in meta-analysis

Outcome type	Outcome subtype	Time frame	Study	Intervention	Control	Odd Ratio (95% CI)	P value
Cardiac risk factors	Achieving total cholesterol	MT	Jorstad et al. 2013	280/358	247/352	1.53 (1.09, 2.14)	0.01
Cardiac risk factors	Achieving HDL> 1mml/L	MT	Jorstad et al. 2013	242/358	233/352	1.07 (0.78, 1.46)	0.69
Cardiac risk factors	Achieving HDL> 1mml/L	LT	Jorstad et al. 2013	243/358	237/348	0.98 (0.72, 1.35)	0.91
Cardiac risk factors	Achieving HDL mmol/L	LT	Saffi et al. 2014	43 (8) n=38	43 (9) n=36		1.00

Outcome type	Outcome subtype	Time frame	Study	Intervention	Control	Odd Ratio (95% CI)	P value
Cardiac risk factors	Triglyceride mmol/L change	MT	Jorstad et al. 2013	-0.1 (1.1)	-0.003 (0.8)		0.22
Cardiac risk factors	Triglyceride mmol/L change	LT	Jorstad et al. 2013	-0.01 (0.9)	-0.03 (0.8)		0.71
Cardiac risk factors	LDL cholesterol change	MT	Jorstad et al. 2013	-0.1 (1.0)	-0.05 (0.9)		0.21
Cardiac risk factors	LDL cholesterol change	LT	Jorstad et al. 2013	-0.1 (1.0)	0.03 (0.8)		0.16

Table 4 Results on smoking cessation from studies were not included in meta-analysis

Outcome type	Outcome subtype	Time frame	Study	Intervention	Control	Odd Ratio (95% CI)	P value
Health behaviours	Smoking cessation	ST	Jolly et al. 1999	37/78	35/76	0.97 (0.69-1.36)	0.49
	Smoking cessation	MT	Jolly et al. 1999	16/85	17/84	1.08 (0.58-1.98	0.46
	Smoking cessation	LT	McHugh et al. 2001	12/27	1/20	0.11 (0.02-0.80)	0.01
	Smoking cessation	ST	Park et al. 2017	3.17(0.82) n=32	2.95(0.84) n=31	0.22 (-0.19-0.63)	0.29
	Smoking cessation	MT	Park et al. 2017	2.92(0.96) n=31	2.85(0.89) n=31	0.06 (-0.40-0.52)	0.80

Table 5 Results on medication adherence from studies were not included in meta-analysis

Outcome Type	Outcome subtype	Time frame	Study	Intervention	Control	Odd Ratio (95% CI)	P value
Medication adherence	Ace-inhibitor	MT	Jorstad et al. 2013	209/358	162/352	1.65 (1.22-2.21)	0.001

Outcome Type	Outcome subtype	Time frame	Study	Intervention	Control	Odd Ratio (95% CI)	P value
Medication adherence	Antiplatelet	MT	Jorstad et al. 2013	354/358	352/354	0.50(0.09-2.75	0.43
Medication adherence	Beta-blockers	MT	Jorstad et al. 2013	296/358	285/352	1.12(0.77-1.64)	0.55
Medication adherence	Statins	MT	Jorstad et al. 2013	345/358	337/352	1.18(0.55-2.52)	0.67
Medication adherence	Calcium-channel blockers	MT	Jorstad et al. 2013	82/358	58/352	1.51(1.04-2.19)	0.03
Medication adherence	Calcium-channel blockers	LT	Jorstad et al. 2013	77/355	65/348	1.21(0.83-1.74)	0.32
Medication adherence	Statins	MT	Jorstad et al. 2013	74/358	53/352	1.47(1.00-2.17	0.05
Medication adherence	Statins	LT over 18 months	Lapointe et al. 2006	50/56	49/55	1/02(0.31-3.38)	0.97

Table 6 Results on anxiety and depression from studies not included in meta-analysis

Outcome Type	Outcome subtype	Time frame	Study	Intervention	Control	Odd Ratio (95% CI)	P value
Health-related quality of life	Depression (HADS tool)	MT	Barley et al. 2014	10.3(3.8) (n=35)	9.2 (4.6) (n=39)	1.10 (-0.82, 3.02)	0.26
Health-related quality of life	Depression (HADS tool)	MT	Barley et al. 2014	10.3(3.8) (n=35)	9.2 (4.6) (n=39)	1.10 (-0.82, 3.02)	0.26
Health-related quality of life	Depression (PHQ9 tool)	ST	Barley et al. 2014	14.8(6.4) (n=41)	13(6.8) (n=40)	1.80 (-1.08, 4.68)	0.22
Health-related	Depression (PHQ9 tool)	MT	Barley et al. 2014	13.4(7) (n=37)	11.7(6.5) (n=40)	1.70 (-	0.27

Outcome Type	Outcome subtype	Time frame	Study	Intervention	Control	Odd Ratio (95% CI)	P value
quality of life						1.32, 4.72)	
Health-related quality of life	Depression (PHQ9 tool)	LT	Barley et al. 2014	12.6(7.1) (n=32)	12 (6.9) (n=37)	0.60 (-2.72, 3.92)	0.72
Health-related quality of life	Depression	LT over 4 years	Murchie et al. 2004	30 (6) (n=481)	36 (8) (n=564)	-6.00 (-6.85, -5.15)	P < 0.00001