Outcomes of Nurse Practitioner Led-Care in Adult Patients with Atrial Fibrillation

by
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Abstract

Atrial fibrillation is the most common arrhythmia and is increasing in prevalence worldwide. While it is not acutely life threatening, the complications of stroke and heart failure carry high mortality rates and extensive healthcare costs. Healthcare leaders have identified the extra demands these places on an already overwhelmed healthcare system and thus new models of care are being assessed. Nurse practitioners are graduate prepared, independent healthcare providers who have a scope of practice, which includes, patient history and physical assessment, ability to diagnose, order diagnostic testing and determine a treatment care plan. They also have prescriptive authority. Thus, utilizing nurse practitioner-led care may be an effective way to improve access to care and patient reported outcomes. This thesis is focused on identifying the benefits of cardiovascular nurse practitioner-led care.

This thesis includes two studies. Study number one is a systematic review and meta-analysis to assess randomized controlled trial evidence determining the impact of nurse practitioner-led care. Our initial search identified 605 potential articles however, only five studies met the inclusion criteria. While none of the five studies reported a statistical difference in health related quality of life and length of stay. Between nurse practitioner-led care and usual care for 30-day readmissions, the limitations of the studies did not provide conclusive evidence of appropriate models of care for patients with atrial fibrillation. Therefore the second study is a randomized control trial assessing the effect of nurse practitioner-led care on health-related quality of life in adult patients with atrial fibrillation. The study is currently ongoing, with a projected end date of December 31, 2019. We have completed an interim analysis for the purposes of this study.

Preface

Chapter 2 of this thesis has been published as**:** Smigorowsky MJ, Norris CM, McMurtry MS, Tsuyuki RT. Measuring the effect of nurse practitioner (NP)-led care on health-related quality of life in adult patients with atrial fibrillation: study protocol for a randomized controlled trial. Trials. 2017;18(1):364. I was responsible for the initial design and manuscript composition.

Chapter 3 of this thesis has been accepted for publication by the Journal of Advanced Nursing.: Smigorowsky MJ, Tsuyuki RT, McMurtry MS, Norris CM. A systematic review and meta-analysis of the outcomes of care by nurse practitioners in adult inpatient and outpatient cardiovascular care. I was responsible for the initial design, collection and analysis of the data, and manuscript composition.

Chapter 4 is original work by Marcie Jayne Smigorowsky. The research project, of which this thesis is a part, received research ethics approval from the University of Alberta Research Ethics Board, Project Name The Effect of Nurse Practitioner Led-Care on Health Related Quality of Life of Adult Patients with Atrial Fibrillation No. Pro00055990, October 28, 2015 (Currently approved until August 19, 2019). I was responsible for the initial design, intervention, collection and analysis of the data, as well as the manuscript composition.

Dedication

This is dedicated to the patients who participated in this study. Their willingness to try a new model of care at a difficult time in their life is very appreciated.

I would also like to mention my father whose support never wavered, nor his belief I would finish my doctoral studies.

Acknowledgements

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I would also like to acknowledge Dr. Alfredo Pantano who instilled my interest in atrial fibrillation and has always been so generous and kind, sharing his knowledge and love of atrial fibrillation. Dr. Tomasz Hruczkowski and Dr. Roopinder Sandhu have also been instrumental helping me become a proficient atrial fibrillation clinician. By collaborating with me in clinic, sharing your knowledge and expertise, you enhanced my skills and knowledge immensely.

The EPICORE team has been invaluable to me with this project. They have been so willing to share their knowledge, support, and always time for laughter. Thank you so much to Glennora Dowding, Yazid Al Hamarneh, Bo Pan and Lily Yushko.

This journey has been filled with laughter, joy, sadness, setbacks, rewards and tons of learning. My intentions when I first set out to complete doctoral studies were altered many times. The support and belief in me by my committee members, colleagues, friends and family has been amazing and I realize I could not have finished my doctoral studies without you. My family suggests I should strongly consider new ways to fill my time.

Lastly, I would like to acknowledge the support of the University Hospital Foundation who believed in this research project and granted me The TD Fellowship Award.

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List of Abbreviations

AD: Anxiety/Depression

AF: Atrial Fibrillation

AFEQT: Atrial Fibrillation Effect on Quality of Life Survey

ANCOVA: Analysis of covariance

CCS: Canadian Cardiovascular Society

CCS- SAF: Canadian Cardiovascular Society Severity in Atrial Fibrillation

CI: Confidence Interval

CSQ: Consultation Satisfaction Questionnaire

CV: Cardiovascular

EASE: Cardiac Ensuring Access and Speedy Evaluation

EP: Electrophysiology

EPICORE: Epidemiology Coordinating and Research Centre

GI: Gastrointestinal

GRADE: Grading of Recommendations Assessment, Development and Evaluation

HF: Heart failure

HRQOL: Health related quality of life

LDL: Low density lipoprotein

MID: Minimally important difference

MJS: Marcie Jayne Smigorowsky

MO: Mobility

NP: Nurse Practitioner

PD: Pain/Discomfort

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

QOL: Quality of life

RCT: Randomized control trial

REDCap: Research Electronic Data Capture system

RN: Registered Nurses

SC: Self care

SD: Standard deviation

SPIRT: Standard Protocol Items: Recommendations for Interventional Trials

SR: Systematic Review

UA: Usual activities

Chapter 1:

1.1 Introduction

Canada's commitment to quality healthcare started with the adoption of Medicare in 1966. This began the ongoing progression of healthcare reforms including changes for sustainability, improved access and quality of care for patients (1). However, aging populations and increasing prevalence of chronic diseases, such as atrial fibrillation (AF), have limited the impact of additional resources dedicated to healthcare reform (2). Therefore, in recent years, new ways of providing healthcare have been encouraged, such as development of multidisciplinary care teams, creation of new roles and utilizing healthcare providers to their full scope of practice [such as nurse practitioners (NPs)]. These new models of care are needed to evolve our healthcare system to meet patient needs (3). Atrial fibrillation is a chronic disease increasing in prevalence resulting in increased demand for limited healthcare resources. Utilizing NP-led-care may increase access and quality healthcare for this burgeoning patient population.

Atrial fibrillation is a chronic disease increasing in both prevalence and incidence (4). While AF is not acutely life threatening, it leads to heart failure and stroke. Both conditions can increase mortality and result in significant costs to the healthcare system if not treated expeditiously (5). Patient outcomes for patients with chronic disease have been shown to improve if care is provided with collaborative teams (6). As the burden of AF has increased various models of care have been utilized to meet patient demands, including NP-led care (7).

The NP role was implemented in the early 1970s and has been utilized in many different healthcare settings including cardiovascular care areas (8). NPs are registered nurses who have attained a Master of Nursing, which enables them to be prescribers of care and perform tasks that

have typically been associated with physicians (9, 10). This advanced education equips NPs with the knowledge and skills to autonomously diagnose, order and interpret diagnostic tests, prescribe treatment, and perform specific procedures within their legislated scope of practice (11). This unique skill set, is what helps to make NP-led care distinctive from registered nurses and other health care professionals (12).

NP practice is holistic in nature and considers patients as whole beings and addresses specific health concerns as well as related interacting mental, spiritual, social, and environmental factors (13). This is apparent in the *Schuler Nurse Practitioner Practice Model* (9) an early model of NP practice that reflects nursing's metaparadigm concepts and views the patient holistically. The model acknowledges patients as active partners in their own care and incorporates wellness, illness, prevention, health promotion, self-care and education into patient care and management (Shuler & Davis, 1993).

NPs work in many different care settings including inpatient and outpatient hospital settings. While NPs are autonomous, the benefits of the role are enhanced when working with other health care professionals. Some of the identified benefits of NP-led care include high quality management of chronic disease as well as improving access to care by decreasing wait times (14, 15). Patient satisfaction is also higher, which may be associated with the fact that NP's typically spend more time with patients (16, 17).

Understanding where the roles have been implemented and the associated benefits for patient care would help to inform the development of other NP roles and identify gaps in the evidence. While there has been a slow adoption of NP-led-care, there are some known benefits and it is probable that utilizing NP-led care could improve access to care for patients with AF as

well as contribute to other possible patient outcomes. This assumption was the trigger for our conduct of a systematic review (Chapter 2) and a randomized controlled trial comparing NP-led care vs. cardiologist care for patients with atrial fibrillation (Chapters 3 and 4 of this thesis).

The following three chapters are a compilation of the aforementioned work (one published peer-reviewed paper, one accepted with changes by a peer-reviewed journal and one interim-analysis paper) completed towards attainment of my PhD. The first paper is the study protocol for the randomized controlled trial, *Measuring the effect of NP-Led-care on health-related quality of life in adult patient with atrial fibrillation*. This paper is published in the journal *Trials*. Nurse practitioners provide care to cardiovascular patients and new roles are being developed, but what are the associated patient outcomes? As such, the second paper is a systematic review of randomized controlled trials determining the impact of NP-led cardiovascular care. This paper has been submitted to the Journal of Advanced Nursing and we have responded to the first round of reviewers' comments.. The third paper is the interim study results paper for *The effect of NP-Led-care on health-related quality of life in adult patient with atrial fibrillation*. This represents a work in progress, with 81 patients enrolled at the time of the writing of this document. The final chapter is the summary, conclusion and recommendations.

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Chapter 2: Measuring The Effect of Nurse Practitioner-Led Care on Health-Related Quality Of Life in Adult Patients With Atrial Fibrillation – A Randomized Trial: Protocol

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2.1 Background

Atrial fibrillation (AF) is the most common arrhythmia and it is increasing in prevalence in a growing and aging population (1). Currently in Canada, there are approximately 350,000 people living with AF (2), but this number is expected to rise. Many countries are experiencing a healthcare crisis, including Canada (3-5). Increasing healthcare demands in an already overwhelmed system require new methods of care delivery to be examined.

Atrial fibrillation is a chronic disease associated with devastating complications like stroke and heart failure (6). Patients with AF have a 3-5 times greater risk of stroke, with strokes typically larger and associated with higher mortality compared to patients without AF(1). There are evidence-based guidelines for treatment for AF in Canada (6) that promote evidence-based practice and improved patient outcomes, including improved quality of life and symptom control. Early intervention and individualized assessment are fundamental for optimal AF management.

Currently, healthcare in Canada utilizes more than 40 per cent of all government funding (7), and these costs are judged to be unsustainable (8). Estimates indicate AF hospitalizations cost the Canadian healthcare system $815 million, with most costs driven by poorly managed AF (9). In addition, projections suggest there will be a dramatic inability to meet the future demand

for health care traditionally provided by a physician (10). These fiscal and demographic realities support that new models of care need to be evaluated.

Nurse practitioners (NPs) are highly trained clinicians and independent healthcare professionals who work in collaboration with other members of the healthcare team to manage a patient's full spectrum of healthcare needs (11). In Alberta, "NP" is a protected title with the scope of practice legislated pursuant to the Health Professions Act. NPs provide comprehensive health assessment, diagnose, treat and manage disease, within a holistic model of care (11). Each NP is accountable to determine their own expertise level of specific competencies and when it is appropriate to involve or refer to other health care providers (12).

Patients are often more satisfied with NP-led care than physician-led care (13, 14). This may be related to NPs spending more time with patients engaging patients in individualized treatment options through patient education and counseling (15). NP patient-centered care may also improve adherence to treatment plans (16-18). NP care also may improve clinical and patient reported outcomes as well as substantive cost savings (19-30). However, despite potential advantages, there are often barriers to broad adoption of NP-led care in many environments (31).

There has only been one randomized control trial to assess nurse-led care vs. standard physician care for patients with AF. A Dutch outpatient hospital clinic randomized 714 patients with AF into 2 equal groups for 2 years(32). The control arm included a 20-minute initial cardiologist consult and 10 minute follow up appointment as required. The intervention arm was an initial consultation in the nurse-led clinic with diagnostic testing completed prior to the visit. Treatment was guided by AF specific decision support software. At the end of the consult a cardiologist would review the patient and care plan. Follow up was at 3, 6 and 12 months and

then every 6 months after. The primary endpoint, a composite of cardiovascular hospitalization and cardiovascular death, occurred in 14.3% in the nurse-led group, compared to 20.8% in the usual care group (hazard ratio: 0.65; 95 % CI 0.45-0.93; p=0.017). Cardiovascular death occurred in 1.1% of the nurse-led care vs. 3.9% in the usual care group (hazard ratio: 0.28; 95% CI:0.09-0.85; P=0.025). Cardiovascular hospitalization occurred in the 13.5% in the nurse-led care vs. 19.1% in the usual care group (hazard ratio: 0.66; 95% CI: 0.46-0.96, P=0.029). Adherence to clinical guidelines was significantly higher in the nurse-led care group. The study concluded that nurse-led care for patients with AF was superior to usual care provided by a cardiologist in this setting. Some important limitations to the study were that complex patients were excluded from participating in the study, and that a cardiologist was still required to review the patient's care. Important remaining questions include whether other outcomes are improved, such as health related quality of life the patient's perception of the quality of care received, and whether a more independent practitioner, such as a NP, would achieve similar results in patients.

The objective of this study is to assess the effect of Nurse Practitioner (NP)-led care on health-related quality of life of adult patients with atrial fibrillation

2.2 Methods/Design

We hypothesize ambulatory patients with AF whose care is managed by an NP will have improved HRQOL as measured by AFEQT scores compared to patients receiving standard care.

2.2.1 Design and Setting

We propose a prospective, randomized control trial (RCT) with 2 equal groups testing for superiority (see Figure 2.1). The RCT will be conducted in the Cardiac EASE Clinic, a multidisciplinary, general cardiology outpatient referral clinic in a large tertiary care hospital in Alberta (33). The clinic's normal practice is for patients to be triaged by RNs who follow

algorithms based on American Heart Association and Canadian Cardiovascular Society (CCS) guidelines. Diagnostic testing is completed prior to the initial clinic visit to decrease time to follow-up. Patients are assessed in clinic by either an RN or Doctor of Pharmacy AND cardiologist, or solely by a NP. Follow-up, if required is either in the cardiologist's own clinic or the NP clinic. Patients who do not require follow up will be returned to their family physicians care. The hospital utilizes an electronic medical record, which incorporates scheduling of diagnostic testing, clinic appointments and communication (letters, patient's health history). In the context of this study proposal, "standard care" refers to regular clinic processes as described above.

2.2.2 Study Population

All adult patients who are referred for assessment for AF to the EASE clinic will be asked to participate in the study. Inclusion criteria are 18 years or older, documented AF, able to provide informed consent and able and willing to complete the study questionnaires on their own or with assistance.

Exclusion criteria are patients referred for AV node ablation or pulmonary vein isolation, patients who have failed rate control or antiarrhythmic medications, or have moderate to severe mitral or aortic valvular heart disease. Patients with unstable AF or who cannot or are unwilling to attend follow up appointments are also excluded. Study criteria will be reviewed with Cardiac EASE RNs on an ongoing basis to assist with study recruitment.

2.2.3 Randomization

After verbal consent is obtained during the telephone triage call, the RN will randomize patients on a secure website. Blocked randomization (using variable block sizes) will be used to ensure there are equal participants in the intervention and control groups and further conceal

allocation. The patient will be scheduled in the determined clinic within 4-6 weeks from date of referral, consistent with CCS guidelines.

Prior to the initial clinic visit, written consent will be obtained by a research assistant along with the baseline questionnaires. Questionnaires will also be completed at 3 and 6 month in-person follow up appointments. If the patient is not being seen in follow up, the questionnaires will be mailed to them. Patients will receive telephone reminders in 2 and 4 weeks if the questionnaires have not been returned.

2.2.4 Intervention

The intervention group will receive NP-led care. The initial visit is with an experienced NP with extra training in AF management. A complete baseline history and physical will be completed to determine a plan of care based on current CCS AF Guidelines. CHADS2/CHADSvasc score (34) will be calculated to identify risk of stroke for each patient. To assist with determining risk for increased potential for bleeding the HAS-Bled score (35) will be calculated. CCS SAF scores(36) will also be completed to identify symptom severity of AF. If the patient develops heart failure, medication intolerances (which limit medical management), requires assessment for treatment with amiodarone, electrical cardioversion or pulmonary vein isolation, or other serious complications, a cardiologist will be consulted. The NP will also provide individualized patient education ("what is AF", "AF management and complications"). Patients will be given a written treatment plan at the end of the consult to assist with patient compliance, self-management and knowledge retention. Patients will also be provided with clinic contact information for future needs.

The NP will see the patient in follow-up at three and six months however, if the patient's condition requires closer follow-up, timing will be adjusted and documented. The patient's

history will be reviewed to determine if they have been hospitalized or had any major adverse cardiovascular events. A provincial electronic medical record will also be reviewed for prescribed medications, dates of hospitalizations and emergency room visits, laboratory blood work results (e.g., INR, troponin, BNP, hemoglobin), and diagnostic tests (echocardiogram, chest x-rays, medical consultations, CT scan and 12 lead ECG tracings).

The control group is standard care by a cardiologist in the EASE clinic. The cardiologist will determine AF management and follow up requirements as per their usual practice. The patient's care will be referred-back to the family physician if no follow-up is required. The schedule of enrolment, intervention and assessments of the complete study protocol (according to the SPIRIT checklist) is shown in Figure 2.2.

2.2.5 Outcomes

The primary outcome is the difference in change in AFEQT scores from baseline to 3 months and 6 months between the intervention and control groups. AFEQT is an atrial fibrillation-specific questionnaire (37) for use with any type of AF. AFEQT is a simple survey with 20 questions based on a seven-point Likert scale covering 3 domains. The questionnaire should take about 5 minutes to complete. Four questions assess AF related symptoms, 8 questions evaluate daily functioning and 6 questions evaluate AF treatment concerns. Two questions assessing satisfaction with treatment are not included in the overall score. Questions 1-18 are included in the overall scoring of the questionnaire. A score of zero corresponds with complete disability while a score of 100 corresponds to no disability. AFEQT has been shown to have good reliability, test–retest reliability, construct validity, and responsiveness as well as discriminatory properties between clinically different groups(37). The lowest global score is

associated with the patients with severe symptoms related to AF. AFEQT has also been shown to be responsive to change (37).

Secondary Outcomes include:

a) difference in change in EQ-5D (general quality of life measure) from baseline to 6 months between intervention and control groups. The EQ-5D is a simple 5 question general quality of life (QOL) questionnaire. It assesses 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. It also has a visual analogue scale for patients to self-rate their overall health. A utility of 1 represents full health while a utility of 0 represents a state equivalent to death(38).
b) difference in composite outcomes of death from cardiovascular causes, cardiovascular hospitalization and emergency room visits between the intervention and control groups. (For ischemic stroke, heart failure, acute myocardial infarction, systemic embolism, major bleeding, severe arrhythmic events and life-threatening adverse effects of drugs*)*. Dr. S. McMurtry will chair a blinded committee to determine this outcome.
c) satisfaction with healthcare provider care will be assessed as measured by the overall mean score of the CSQ completed at the 6-month follow-up visit. The CSG is a self-administered tool based on 18 questions with a 5-point Likert scale ranging from strongly agree to strongly disagree(39). There are 3 factors: 1) professional aspects of the consultation, 2) depth of patient relationship, 3) perceived length of consultation. There are 3 questions related to overall general satisfaction. Higher scores indicate higher satisfaction.

2.2.6 Sample Size

After a review of the literature for AFEQT, a minimally important difference (MID) score for change was not identified. In the initial validation study (37), the standard deviation (SD) for change from baseline to 3 months in the medically managed group was 20.0 (overall AFEQT global score). This group is most like the projected population for this study and was therefore utilized as the standard deviation for sample size calculations. We consulted Dr. Paul Dorian, an experienced arrhythmia specialist, AF QOL researcher and co-author of the AFEQT questionnaire, who suggested the MID for AFEQT was 12. As such, we chose an effect size of 12, i.e., NP-led care would improve AFEQT scores by at least 12. A sample size of 64 participants in each group will detect a MID of 12 in AFEQT scores (SD 20, two tailed t test, 80% power and significance level of 5%). 70 patients per group (total 140) will be recruited to allow for 10% loss to follow up.

2.2.7 Statistics

All sociodemographic and clinical characteristics for the intervention (NP-led care) and control group at baseline will be summarized using means $\pm$ SD for continuous variables; and the observed number and percentages for categorical variables. For the main outcome, ANCOVA will be used to assess change in AFEQT scores over time: baseline to 3 months and 3 months to 6 months (repeated dependent measures) in both intervention and control groups. ANCOVA assumes normal distribution of the data as well as homogeneity of variance and the groups being balanced. Adjusting for pre-test scores will identify that the post intervention difference in scores is truly a result of the intervention. ANCOVA will also account for variation around the post-test means that comes from the variation attributed to the patients AFEQT scores started at baseline. Previously, it has been shown with other HRQOL scores that data can be skewed due to ceiling or floor effects resulting from extreme values and non-equal distances between values on ordinal

scales(40). However, the Central Limit Theorem states the means will be normally distributed regardless of the original distribution when there are at least 30 per group(41). This study is projected to have 2 equal groups with 70 participants. If the initial data analysis reveals non-normal distribution and skewed data, further analysis will be completed to determine if transformation of the data is required or if other statistical analysis would be more appropriate. An independent t test will be utilized to assess the difference in means between NP care and physician led care. Kaplan-Meier survival analysis will be utilized to evaluate the composite endpoint of cardiovascular death and hospitalizations determined by blinded assessors. Multivariate analysis will be used to adjust for possible differences in baseline characteristic and scores for any significant variables. Consultant satisfaction will be determined by comparing the means with independent t tests. A p value of less than 0.05 will be considered statistically significant. All analysis will be based on the intention to treat principle.

Missing data will be replaced with the overall mean of the missing variable. This technique is known to accurately identify the mean but will underestimate the SD making the confidence interval overly optimistic(42) however other options also have imperfections. This will need to be considered in the final analysis. All analysis will be performed with the latest version of SPSS statistical software.

Data entry will be completed in a mature, secure web application specifically developed for surveys and databases. An application is specifically designed for this study with limits built into data entry fields to limit errors. Data entry will be completed by M. Smigorowsky with random data entry checks by a specific EPICORE Centre staff member. Final data set will only be available to M. Smigorowsky and a specific EPICORE Centre staff member. We did not feel that a Data monitoring committee was needed for the following reasons: First, the NP

intervention is already part of how care is delivered at our institution. We are simply evaluating it. Secondly, as a trial of a treatment approach, we did not feel that data monitoring would be necessary (and our research ethics board did not require it).

2.2.8 Ethical Considerations

This research protocol has been approved by the Health Research Ethics board at the University of Alberta. The patients will be required to read and understand the clinical trial information sheet and provide consent to participate. All patient information and study questionnaires will be treated with confidentiality and locked in a secure data storage facility at EPICORE Centre (www.epicore.ualberta.ca). All information will be de-identified to maintain confidentiality. Modifications to any part of the study protocol will be resubmitted to the Health Research Ethics Board at the University of Alberta. Participants will be notified if applicable.

2.3 Discussion and Design Issues

Currently there is little evidence identifying a model of care that is sustainable and improves the QOL in patients with AF. There are several known benefits of NP-led care within other chronic disease states(23-25) and it is therefore reasonable to assume similar benefits could be attained with NP-led care for AF patients. NPs are independent practitioners working collaboratively with physicians and therefore the potential exists to decrease wait times for patients to be seen. This is extremely important for stroke risk assessment, or to re-evaluate patients with increasing symptoms to adjust medication regimes or arrange for interventions such as cardioversion or EP interventions. Both interventions have the potential to make a strong impact on patient outcomes but also on the health care system limiting emergency room visits and hospital admissions. Earlier appropriate management should also produce fewer devastating, costly complications of stroke and heart failure. Some Canadian centers already utilize RN or

NPs in their clinic, but without complete evidence of their effectiveness. Our proposed trial will help evaluate a framework of care and determine the impact on HRQOL.

We have chosen to conduct a superiority RCT instead of a non-inferiority design because we feel that NP care may offer some important patient focused advantages over that of usual physician-based care. The primary outcome is a patient important outcome rather than a clinical outcome (had we wished to evaluate clinical outcomes, we agree that it would be reasonable to design a non-inferiority trial of NP-led care vs. standard care). NP-led care, as alluded to earlier, has been consistently shown to rate higher on patient satisfaction. This may in part be due to the holistic model of care followed by NPs. It engages patients in their healthcare plans and addresses other psychosocial areas which may have an impact on their health. Ultimately this may have an impact on their HRQOL, the primary outcome for this study.

The control group is usual care. In our case, patients are seen by a general cardiologist and the details of the intervention and follow up are left to the individual cardiologist. We make no attempt to protocolize this, it is truly usual care and we feel that it is generalizable to the Canadian setting.

This research study is supported by the Cardiovascular Heath and Stroke Strategic Clinical Network (which is a network of professionals working towards better quality and outcomes for cardiovascular health in Alberta. Results will be presented and published at conferences and journals appropriate for research on AF and NP roles. Plans will also be made to share findings with Alberta healthcare leaders and staff to support change in clinical practice if NP-led care is shown to be beneficial

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Figure 2.1 – Protocol Flow Chart

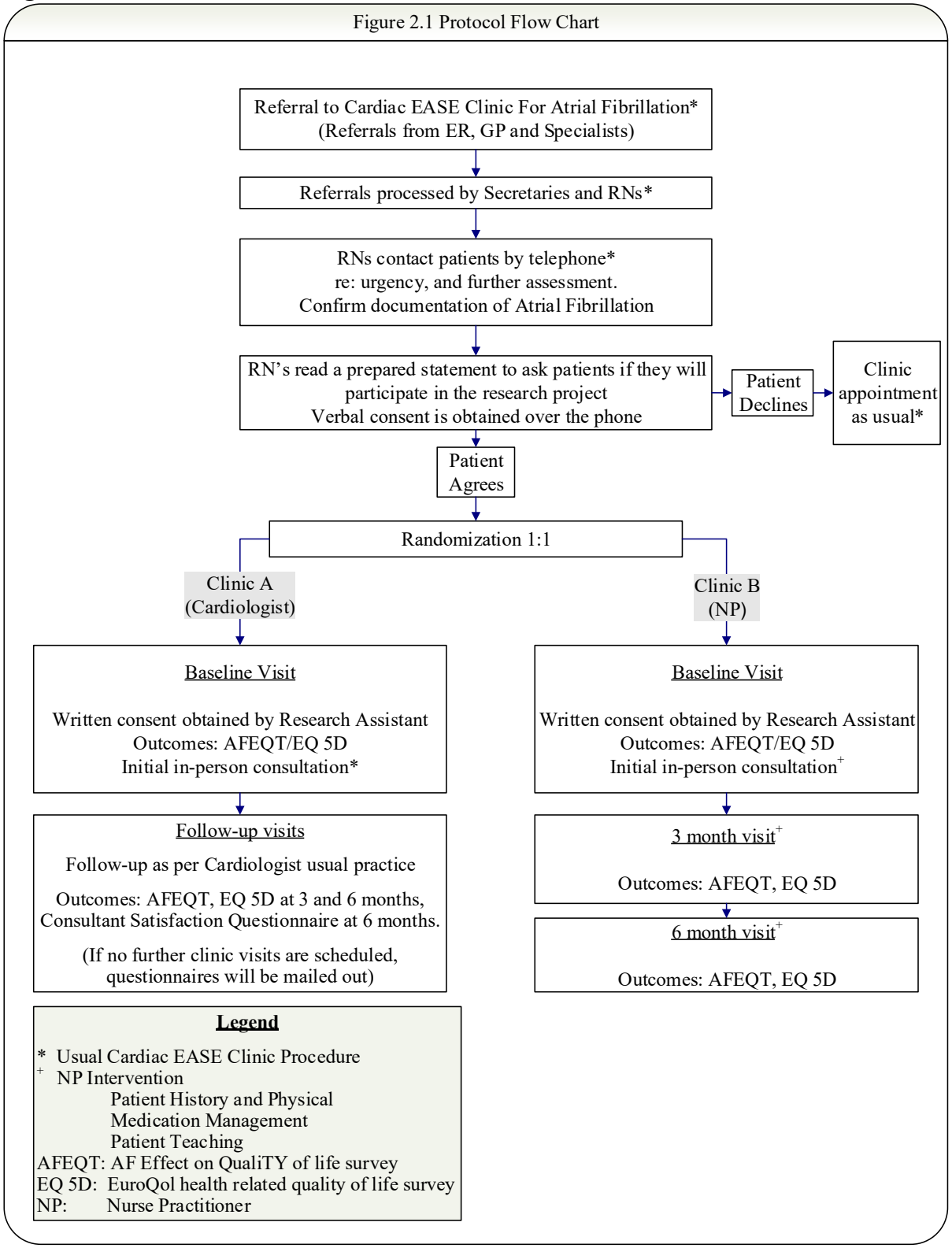

Figure 2.2 Spirit Diagram

	STUDY PERIOD							
	Enrolment	Allocation	Post-allocation					Close-out
TIMEPOINT**	$-t_1$	0	t_1	t_2	t_3	t_4	etc.	t_x
ENROLMENT:								
Eligibility screen	X							
Informed consent	X							
[List other procedures]	X							
Allocation		X						
INTERVENTIONS:								
[Intervention A]			←	—	→			
[Intervention B]			X		X			
[List other study groups]			←	—	—	→		
ASSESSMENTS:								
[List baseline variables]	X	X						
[List outcome variables]				X		X	etc.	X
[List other data variables]			X	X	X	X	etc.	X

Chapter 3: A systematic review and meta-analysis of the outcomes of care by nurse practitioners in cardiovascular care.

A version of this study has been accepted by the Journal of Advanced Nursing for publication: Smigorowsky, M.J., Tsuyuki, R.T., McMurtry, M.S., & Norris, C.M., A systematic review and meta-analysis of the outcomes of care by nurse practitioners in cardiovascular care.

3.1 Introduction

Health care reform is occurring internationally, rooted in important issues such as reducing healthcare costs, wait times for appointments and procedures, as well as improving quality of care and patient safety(1). While healthcare reform has been occurring for the last twenty years there are two parallel issues which contribute to barriers for swift and successful change. Globally, most countries have an aging population and burgeoning growth of people living with chronic diseases (2). Individually and together, these two health issues continue to increase utilization further taxing increasingly limited healthcare resources worldwide.

The demands of aging populations, along with the associated increased prevalence of chronic disease and sky rocketing costs are creating ongoing challenges to healthcare sustainability (3). Healthcare leaders and providers are therefore looking for new innovative models of care to provide safe and affordable patient care. A question often asked; why use one healthcare provider role over another? With limited healthcare dollars, leaders have to make justifications to determine which model of care to use. Healthcare leaders are encouraged to utilize healthcare data and outcomes to inform difficult decisions; such as utilization of healthcare providers(4). In Canada(2)Australia (5), United Kingdom(6) and the United States(7) there is growing support for all healthcare providers to work to full scope of practice and therefore it is essential to clearly outline the benefits of specific role**s.**

Internationally, nurse practitioners (NP) are graduate-level prepared registered nurses (in most countries), whose scope of practice includes health maintenance and promotion from diagnosis, treatment, to follow-up of patients with acute and chronic conditions in both the inpatient and outpatient setting(8, 9). Nurse practitioners are independent practitioners, who may work in collaboration with other healthcare team members. They are unique in that NPs utilize select medical skills as well as advanced nursing skills which may provide benefits to patients and the healthcare system such as decreased costs, increased patient engagement with their care and improved quality of life(10).

Currently NP-led care and the associated outcomes of care in different care areas have not been broadly evaluated. Randomized controlled trials are the gold standard to evaluate treatment efficacy (11). Therefore, the purpose of this study was to conduct a systematic review (SR) of randomized control trials (RCT) assessing NP-led cardiovascular (CV) care and associated outcomes of care.

3.2 Background

Nurse Practitioners are registered nurses who have graduate education to enable them to diagnose, prescribe and independently order treatments (8). The NP role was implemented in the late 1960's in the United States(12) and in Canada during the late 1970's (13). The focus of the role initially was in primary care and pediatrics(13, 14) however in the late 1980's the acute NP role was introduced which led to NPs practicing in the hospital setting(15) focusing typically on specialty areas of care such as CV care (16-18). In many tertiary centres, NPs provide care in CV settings within cardiology and CV surgery. Cardiovascular NP's specialize in the diagnosis and treatment of heart disease/abnormalities and post-operative heart surgical care within intensive care, ward settings and ambulatory outpatient clinics.

In other patient care areas, studies have also reported the NP role results in increased patient satisfaction, improved patient outcomes, decreased length of stay and improved health related quality of life (HRQOL)(15, 19-22). A systematic review on the safety and effectiveness of NP-led care in primary care included seven RCT's, two economic analysis and one follow up study. A quality assessment does not appear to have been completed however, they identified NP-led care was associated with equal or slightly better outcomes compared with physician-led care for physiologic measures (e.g., improved BP and cholesterol control) patient satisfaction and cost. NP-led care was associated with slightly longer appointments than physician-led care (23). It was concluded NP-led care was effective and safe. A recent Cochrane Library systematic review was completed evaluating NPs (and other healthcare providers) as substitutes for physicians in primary care(24) which included 18 RCTs. Results bolstered the findings from the Swan et al. systematic review as results were very similar, again finding there is similar or better outcomes between NP-led care and physician led-care for several patient conditions. NP-led care is also associated with increased patient satisfaction, longer consultations, and possibly higher return visits. There doesn't appear to be any difference with hospitals admission, emergency room visits, number of prescriptions filled, and number of tests ordered. While the evidence for primary care NP-led care is growing, there is a gap in the evidence specifically in understanding the specific areas within CV care were NPs currently provide care to patients and the associated outcomes of the roles.

We completed an a priori comprehensive review (literature search January 1980 – February 2017) to try to establish the typical CV NP-led care outcomes. The initial search identified 2040 studies. After title review, the search identified 170 studies (all types) identifying different models of care with significant methodological issues. With the current

interest in utilizing the NP role to full scope of practice, we felt a systematic review of RCTs comparing NP-led care (independent practice) vs other models of care (typically physician-led/standard-care) in any CV setting was required to identify CV NP-led care as a model of care and possible associated outcomes.

Utilizing the full scope of practice of the NP in CV care, may be a well-founded option to meet the increasing demands that the expanding prevalence of CV disease is putting on the healthcare system. Acquiring a better understanding of the types of roles as well as potential clinical outcomes of care will be helpful to healthcare leaders to assist with further development and utilization of NP-led CV care.

3.3 The Review

3.3.1 Aim of Study

This systematic review and meta-analysis aimed to appraise the evidence concerning the effectiveness of cardiovascular nurse practitioner-led care (as a model of care) on the outcomes of care for adult patients in cardiovascular care areas.

3.3.2 Design

A systematic review of RCTs reporting NPs providing care in any CV patient care setting and examining the impact of clinical outcomes of care associated with NP-led care. The guidelines of the Cochrane Collaboration were adopted to carry out this systematic review and meta-analysis (25) and reported using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (26)

3.3.3 Search Methods

A systematic search was conducted to identify all published and unpublished RCTs related to CV NP-led care and associated outcomes of care between January 2007 and July 2017 in the following databases: CINAHL with full text (EBSCO), Ovid EMBASE, Ovid Medline,

ProQuest Dissertations & Thesis Global, Cochrane Library Database of Systematic Reviews and Controlled Trials, Scopus, and Web of Science Core Collection. A librarian familiar with nursing and medical research assisted with developing and conducting the search. Search results were limited to English and relevant references noted in articles reviewed were also assessed. The full search strategy is attached as supporting information. The following combinations of MeSH (Medical Subject Heading) terms or keywords were used: cardiovascular disease, atrial fibrillation, nurse practitioner, randomized controlled trial, cardiology, cardiac surgery, coronary artery disease, high cholesterol, hypertension. Stroke was considered initially, however we felt that it was a separate focus of care and therefore excluded in the title review. Duplicate records and trials were excluded by screening the titles and abstracts. Remaining articles were reviewed to determine if they met inclusion criteria.

3.3.4 Participants

Included patients were > 18 years of age requiring tertiary specialty CV care. The patients had to be randomly allocated to either CV NP-led care or another CV healthcare provider.

3.3.5 Interventions

Patients in the experimental group had to be cared for independently by a nurse practitioner. The description of the intervention had to clearly identify the NP provided patient care to their full scope of practice.

3.3.6 Comparison

The control group received care from another CV healthcare provider (typically physician-led care).

3.3.7 Outcomes

Any reported health systems or patient reported outcomes of care associated with CV NP-led care.

3.3.8 Study Design

Studies needed to be randomized controlled trials that were published in English between the years 2007 and 2017. Limiting the time frame to the last 10 years was pertinent since healthcare delivery has changed over the last 10 years as has increased implementation and acceptance of the NP role in independent care settings(27-29). Studies must also include cardiovascular outcomes of care associated with independent CV NP-led care . Traditionally there has been confusion around the NP role with regards to the utilization of the name and role. It is therefore recommended NP studies where the NP role is not clearly identifiable as working independently to full scope of practice, not be included in research protocols related to NP-led care(30). Therefore included studies had to clearly identify the role functioned as a independent NP working to full scope of practice(31, 32). Limiting to only RCTs was important as we were looking at role effectiveness and felt it was important to find evidence at the highest level as well as the knowledge gained by comparing NP-led care to usual care.

3.3.9 Search outcome

All study references were uploaded to EndNote (X7.8- Clarivate Analytics). The initial search identified 605 studies through the electronic data base search. Duplicate articles were removed. After title review 539 studies were excluded and after abstract review a further 56 studies were omitted as they did not meet the PICO criteria of the review. After full article review, 5 articles meet the SR and meta-analysis inclusion criteria. Reasons for exclusion included: studies were not RCT's, unable to identify the NP role as independent practice, same study but outcomes were reported in separate articles, not CV NP-led care (e.g., primary care)

and abstract only (unable to find published article). The article search outcome flow diagram is presented in Figure 3.1.

3.3.10 Quality appraisal

Risk of bias was determined using the Cochrane Risk of Bias Tool *Cochrane Handbook for Systematic Reviews of Interventions: Version 5.1.0* In Cochrane (Ed.)(25). Previous studies (19) have identified it is not possible to blind participants and personnel to the "NP" intervention, therefore the lack of binding was not considered in the determination of risk of bias. Each study was assessed according to the type of bias and were rated as either unclear risk, low risk or high risk. Studies were then categorized into groups labeled as low risk of bias (at risk in 0-1 categories), moderate risk of bias (at risk in 2-3 categories), or high risk of bias (4-6 categories). 100% of studies had no reporting bias, 60% had no attrition bias, 40% had no detection bias or selection bias. Over all two studies were low risk of bias, two were moderate risk of bias and one was high risk (Figure 3.2, Figure 3.3).

3.3.11 Data extraction

Two authors independently extracted the study data and disagreements were dealt with by consensus. Data extracted included: author, year, country, publication status, sample size, number of patients in each group, inclusion criteria, length of enrollment and follow up, study aims, activities performed by the NP, identified outcomes, NP experience/training and the associated outcomes of care specified in each study were documented on the data extraction form. Identified outcomes included 30-day readmission rate for heart failure, SF-36 physical and mental health scores, length of follow up after cardiac surgery, and vascular risk reduction (Table 3.1)

3.3.12 Synthesis

Studies were assessed to determine outcomes of care associated with NP-led care as a model of care when compared with usual care. We identified four associated outcomes of care but assessed SF 36 physical and mental composite scores as separate outcomes. A separate meta-analysis was completed for each outcome of care to pool results except for vascular risk reduction as there was only one RCT. The effect sizes for length of stay after cardiac surgery and SF 36 physical and mental SF 36 scores, and were estimated as continuous outcomes with 95% confidence intervals, pooling mean difference and standardized mean differences. Effect size for 30-day readmission rates for heart failure (dichotomous) and therefore was estimated with 95 % confidence interval pooling odds ratios. Heterogeneity was assessed by the I^2 statistic. Heterogeneity was determined to be low if the I^2 value was <30(25). We carried out a meta-analysis for NP-led care compared to usual care with the identified associated outcomes. The effects of outcomes associated with NP-led care were calculated using a random effects model to compute the mean difference and standardized mean difference or odds ratio. Forrest plots were produced for 30-day readmission rate for heart failure, length of stay post-operative cardiac surgery and HRQOL as SF 36 physical and mental composite scores(Figure 3-6).

All data was analysed and respective studies were pooled using Review Manager software (RevMan, version 5.3; The Cochrane Collaboration)(33). We conducted a narrative synthesis of the vascular risk reduction outcomes as meta-analysis was not possible. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system (34) was used to assess the quality and strength of the evidence and outcome presented in the "Summary of findings" (Table 3.2).

3.4 Results

3.4.1 Patient characteristics

The effect of NP led care on 30-day readmission rates for heart failure was assessed in two studies (566 patients) from the United States(35, 36). The mean average age in the NP-led arm was 73 years and 70 years in usual care. Gender was fairly equally represented; 44% NP-led care and 51% usual care. Length of stay was assessed in two NP-led post-operative CV surgical RCTs (272 patients) from Canada(37, 38). The mean average age in the NP-led group was 66 years and 65 years usual care. Both genders were included however there was a lower percentage of females; 10% in NP-led care and 18% in usual care. Health related quality of life was evaluated in two studies (406 patients, one from Canada and one from the United States, using the SF 36 questionnaire(36, 38). Age and gender were similar between both groups. Average age in both groups was 68 years and 24% females in NP-Led group and 25% in usual care. The Vernooij study, from the United States, compared NP led-care to usual care to reduce vascular risk factors in patients with clinically manifested vascular disease(39, 40). Total of 638 patients, average age 60 years in the NP-led group and 59 years in usual care group. Majority of patients were males, 78% in the NP-led group and 71% in usual care. In all studies the intervention groups were NP-led care compared to usual care (control group). Table 1 identifies the summary data of the included trials.

3.4.2 Effect of Interventions

We identified 4 outcomes of care associated with NP-led model of care. However, HRQOL was divided in SF 36 physical and mental composite scores. We calculated differences in the effect of outcomes between NP-led care and usual care. To clarify, we were interested in the change in HRQOL between NP-led care and usual care not in comparing HRQOL outcomes

between cardiac conditions. The details of the various outcomes, quality of evidence, and magnitude of the effect are presented in Table 2; Summary of Findings.

3.4.2.1 Effect of NP-led care on 30 day readmission rates for heart failure

Two RCTs involving 566 patients assessed the effect of NP-led care on 30 day readmission rates for heart failure (35, 36). A meta-analysis with a model of random effects revealed NP-led care had no statistically difference (Odds Ratio:0.65, 95% CI: 0.41, 1.04, Z=1.78, p= 0.07) on 30-day readmission rates in heart failure (Figure 3). There is low quality of evidence due to risk of bias (Table 2). I^2 statistic is 7% and indicates risk of heterogeneity is low.

3.4.2.2 Effect of NP-led care on Length of Stay after Cardiac Surgery

Length of stay was assessed in two NP led post-operative CV surgical RCTs (272 patients)(37, 38). The mean difference for length of stay indicates no significant difference between NP-led-care and usual care on length of stay after surgery (mean difference [MD]=-0.89, 95% CI: -2.44, 0.66, Z=1.13, p=0.26,) There is moderate quality of the evidence. One study has a very wide CI. I^2statistic is 0%, indicating low risk of heterogeneity (Figure 4).

3.4.2.3 Effect of NP-led care on SF 36 Physical Composite Score

Two studies with a total of 403 patients investigated the effectiveness of NP-led care on HRQOL(36, 38). The minimal important difference to identify a significant change in the physical composite score has been reported as 5(38). The mean difference [MD]=0.17, 95% CI: -0.89, 1.23; Z=0.32) p=0.75, (Figure 5). No significant difference found. I^2 statistic =0%, suggesting low evidence for heterogeneity. Overall the quality of the evidence is moderate with the decrease in quality due to risk of bias, for SF36 physical composite quality of life scores.

3.4.2.4 Effect of NP-led Care on SF 36 Mental Composite Score

The same two RCTs evaluating SF 36 Physical composite Score (403 patients) also evaluated SF 36 mental composite score(36, 38). The minimal important difference is five which is the amount of changed needed to identify a significant change in the mental composite score. The mean difference for SF 36 mental composite score (mean difference [MD]= -1.11, 95% CI: -4.19, 1.98; Z=0.70, p=0.48 (Figure 6). No statistical difference was found. I^2 statistic is 80% however, we are identifying studies that had NP-led are as a model of care and associated outcomes. We are not comparing HF and post-operative cardiac surgery patients but the change in HRQOL within each study. The quality of the evidence for SF 36 mental composite score is moderate, mostly downgraded for risk of bias.

3.4.2.5 Effect of NP-led Care on Vascular Risk Reduction

The Vernooij study compared NP led-care to usual care to reduce vascular risk factors in patients with clinically manifested vascular disease (Total 330 patients)(39, 40). There is only one study and thus a narrative synthesis has been completed.

A relative change in the Framingham risk score from baseline to one year follow up was assessed as the primary outcome. The NP led-group had a higher Framingham risk score at baseline. Therefore, the baseline Framingham score was adjusted, to produce a relative change of -12% (-22% to -3%). The evidence suggests there is a small benefit of NP led-care to help the patient make necessary lifestyle changes to decrease vascular risk.

Secondary endpoints were absolute changes in the levels of risk factors. 18.4% of patients in the NP -led group reached LDL targets, 19% stopped smoking, as well as a trend was identified for patients receiving NP led-care favoured an improvement in basal metabolic index, triglyceride levels and systolic blood pressure. Overall, NP led-care was found to have a small

benefit to help patients lower certain vascular risk factors, however, they do not appear to report p values.

3.4.3 Publication Bias

There are a limited number of trials assessed in this meta-analysis. The potential for publication bias is therefore not assessed in this systematic review and meta-analysis.

3.4.4 Psychometrics

The SF 36 was utilized to assess HRQOL. The questionnaire has been utilized extensively and is well validated and shown to be reliable and responsive(41)

3.4.5 Quality of the evidence

There is low quality of evidence (due to risk of bias) for no statistical difference in 30-day readmission heart failure rates associated with NP led-care. The quality of the evidence for length of stay is moderate mostly due to imprecision as one study has a very wide confidence interval. Overall the quality of the evidence is moderate with the decrease in quality due to risk of bias, for SF36 physical composite quality of life scores. The quality of the evidence for SF 36 mental composite score is moderate, mostly downgraded for risk of bias. The quality of the study is moderate mostly due to indirectness because they are using a change in Framingham scores to infer vascular risk reduction. The results of the intervention could also be affected by the participants' ability to utilize the website (Table 2).

3.5 Discussion

3.5.1 Summary of Main Findings

With an aging population and strained healthcare systems, utilizing NP led-care has the potential to deliver high quality care to meet CV patient health care needs. However, in this era of constrained healthcare resources, solid evidence is needed to implement new models of care. To this end, we conducted a systematic review of the outcomes of NP led-CV-care. We

identified five RCTs that evaluated a total of 1268 patients across three areas of CV care including heart failure, post-operative CV surgery and vascular risk reduction. We ascertained two patient reported HRQOL outcomes (SF 36 physical and mental composite scores), two outcomes of length of stay after cardiac surgery and 30-day readmission rates in heart failure, and one vascular risk reduction outcome. We therefore conducted four meta-analysis's to analyze the two HRQOL and two systems outcomes related to NP-led CV care. We reported a narrative review of the vascular risk reduction outcomes as there was only one study.

Nurse practitioner-led-care is well-known to be associated with positive outcomes of care in other areas (42). Decreasing 30-day readmission rates for heart failure and length of stay after cardiac surgery have been identified as priority health care reform issues since the early 1970's(43). Nurse practitioner roles have therefore been implemented to assist with achieving these health system goals.

Previously studies have shown CV NP led-care is associated with decreasing 30-day readmission rates for heart failure (44-46), which does not correlate with our findings. We focused on RCTs while the studies that identified reduction in 30-day readmission rates included studies with weaker methodologies (retrospective, improvement project & descriptive). The studies also followed patients for different lengths of time. Blum(36) initially found decreased 30-day heart failure readmission rates however it was not maintained after one year while Estrela-Holder and Zeroth followed patients for six months(44). Rood also found a 30-day readmission rate reduction however patients were followed for 30 days and flaws noted in the research design could contribute to the findings (35).

Our study findings did not identify that NP-led care was associated with decreasing length of stay after cardiac surgery however, Meyer and Miers(47) assessed decreasing length of stay in post-operative CV surgery patients with a retrospective chart review. They compared the previous model of care to current NP led-care. A decrease of 1.91 days' length of stay was found. The studies in our meta-analysis included the Goldie study(37) which was not able to recruit to the full sample size and Sawatzky reported length of stay however it wasn't originally identified as one of the main outcomes of care of the study(38). The trial design therefore may not have been powered or designed to capture length of stay accurately.

When HRQOL is evaluated as an outcome associated with direct NP led-care it has been found to be associated with higher levels of HRQOL scores. However, when HRQOL is assessed as an outcome when NP-led care is compared to another healthcare provider, frequently it has been identified there is no difference in the patient's self-reported health status(48-52). Our review showed no difference in SF 36 physical and mental composite scores associated with CV NP led-care when compared with other healthcare providers which seems to correlate with other research findings.

We found one study identified NP-led-care assists patients to decrease their overall vascular risk by lowering some vascular risk factors(40). This correlates with other research findings where patients in the NP led-group had better control of their cholesterol levels and other risk factors(23, 53-55).

While incorporation of NPs into CV care has been welcome, there is little known about the outcomes of care. Our review of the available evidence shows no significant impact on patient outcomes. The NP role is the most studied health care role (42) however it has previously

been identified, there are many low quality studies and few randomized control trials(19, 56). Our findings also support this and highlights the important need for more investment in high quality research in this important model of healthcare delivery.

3.5.2 Strengths & Limitations

The strengths of this systematic review include using a comprehensive search strategy, rigorously screening and adhering to the PRISMA checklist(57), utilizing established quality assessment tools, and completing the outcomes assessment with GRADE(34). The limitation of this study is that very few studies met the inclusion criteria for this systematic review. The studies that were included were mostly of lower quality.

3.5.3 Recommendations For Future Study

We found that many pertinent abstracts of NP-led-care did not appear to have been developed into a peer reviewed published article. A systematic review of why medical and health-related studies are not being published found the most common reason for not publishing was lack of time or rated as a low priority(58). It has been previously noted NPs find it difficult to balance their clinical role with conducting research(15) which could be a reason for many abstracts not progressing to a published article. Additional employer support or academic mentorship may assist NPs to balance the demands of both roles and enable them to publish important research which is needed to guide practice.

The findings in this review are most likely due to the limited number of RCTs in NP-led CV care as well as study design flaws. Randomized controlled trials provide the strongest level of evidence (59) however, a poorly designed RCT can give misleading results especially if randomization is flawed (60). Randomized controlled trials are more difficult and expensive to conduct which may limit this choice of study design. This finding is not unique to nursing.

Other disciplines also have limited RCTs, in medicine they account for only five percent of studies (61, 62) .

This SR found the risk of bias assessment revealed many randomization issues which determined the higher risk of bias ratings. There were also other design flaws which may have led to our non-statistical findings. When publishing, a very detailed methods section is required to allow for replication as well as to allow the reader to determine if it is pertinent to their patient population(60). Our study findings found intervention details were not always noted and ultimately affected our rating of risk of bias and quality assessment.

All the studies examined were designed and conducted prior to 2013 when SPIRIT was launched as a protocol to help improve the quality of clinical trial protocols. Utilizing the SPIRIT 2013 (63, 64) protocol and checklist when designing and reporting a RCT will help to ensure all important elements of the trial are reported and thus decrease the risk of bias which ultimately will help improve the overall quality of NP-led RCTs. We recommend well designed, high quality RCTs need to be completed in CV NP led care. Nurse practitioners need to ensure completed research be published to establish and document outcomes associated with CV NP led-care. Published evidence should be utilized to drive clinical practice(60).

3.6 Conclusion

This systematic review examined clinical outcomes associated with NP-led CV model of care. After an extensive search, we found a limited number of RCTs. There is predominantly low to moderate quality evidence NP-led CV care has no significant effect on decreasing 30-day readmission rates for heart failure, reducing length of stay in post-operative cardiac surgery, or improving HRQOL scores in this systematic review. Nurse practitioner led-care is associated with a small effect to lower vascular risk. The CV NP role has been increasing, however research

related to the role has lagged behind clinical practice. It is extremely important for further high-quality research to be conducted to identify clinical outcomes of care associated with NP-led CV care as a model of care.

3.7 Reference List

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Figure 3.1: Article Search Outcome

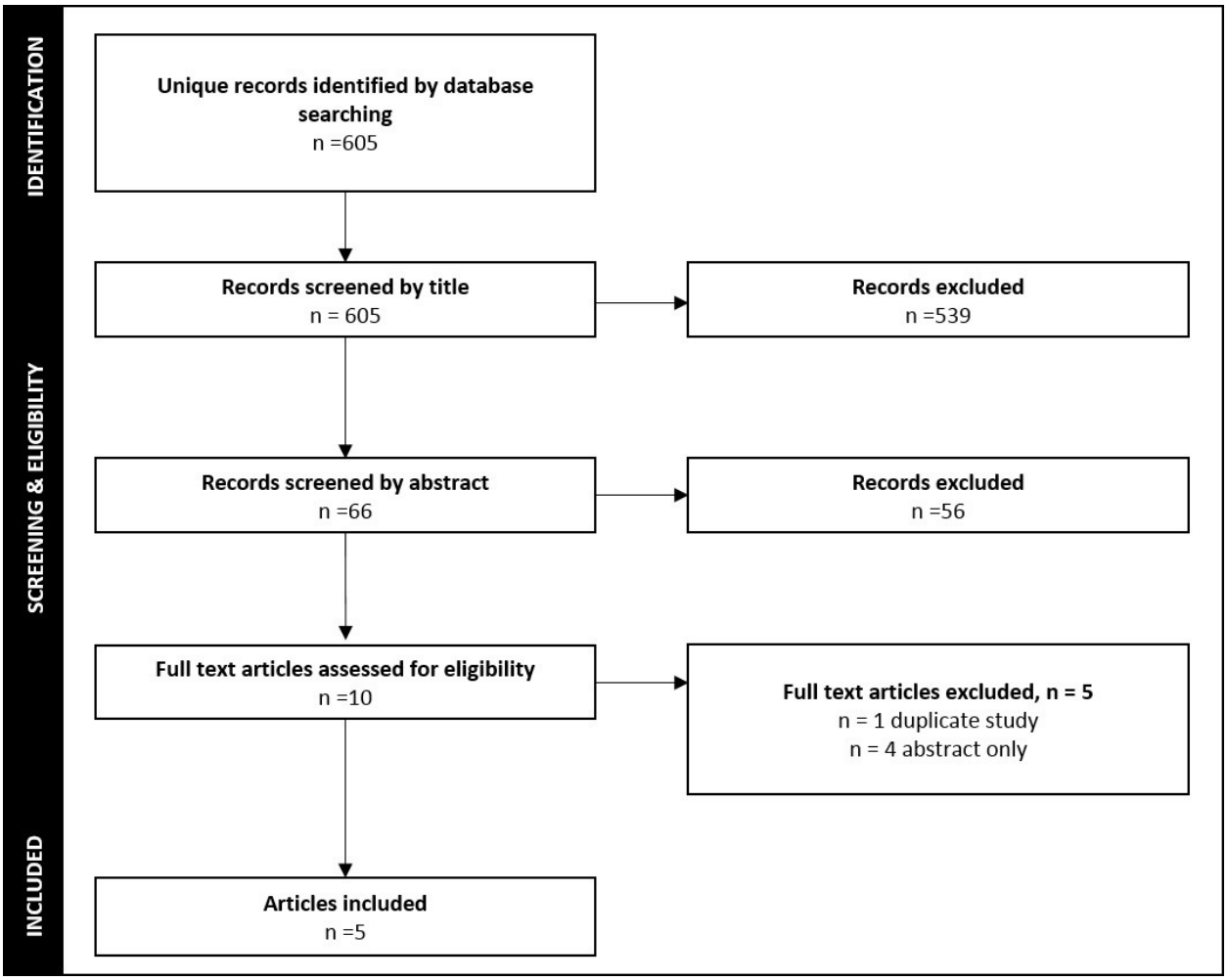


Table 3.1: Summary of Data from Included Randomized Controlled Trials CV NP-Led care vs Usual Care

Author, year, country, additional publication	Sample size/ n=/each group	CV care Area/ Number of sites	Inclusion criteria/ Length of Enrollment/ Length of follow up	Study Aims	Intervention (NP- role)	Selected outcomes study findings for NP-Led Care	Number of NPs/ experience & training
Blum & Gottlieb, 2014, USA	N=206/ NP n= 104/ UC n= 102	-Outpatient HF/ Multisite	-Hospitalized in last year/ -4 years/ -5 years (or until death)	-Reduce hospital & emergency room visits -improve self-care.	- Home monitoring -abnormal, weight & symptom changes treated -assessed by cardiologist as needed	- No difference 30-day readmission rates for HF -No difference SF 36 physical and mental composite score	-One NP -Extensive HF experience
Goldie et al., 2012, Canada	N=103/ NP n= 22 UC n= 81	-Post-operative CV surgery/ -One site	Scheduled for coronary bypass or valve surgery/ -9 months/ -Followed admission to 6-8 weeks' post discharge.	Difference in: length of stay, readmit rates, complication, follow-up, cardiac rehab, patient & team satisfaction	-Followed clinical pathways -Cardiac surgeon consulted as needed	-Didn't achieve sample size -No difference in length of stay post cardiac surgery	-One part time NP -One year work experience on CV unit
Rood, 2014 USA Dissertation pilot project not published	N=48/ NP n= 20 UC n= 28	-Inpatient HF transitioning to outpatient care/ -One site	-HF patients transitioning home/ -3 months/ -30 days	Reduce 30 day readmission rate for HF	- Education & HF management follow up in 3-5 days post discharge -Treated prn for 30 days - Physician prn	-No difference between 30-day readmission for HF - Flaws with trial design	-One extensive HF experience -Formal practice agreement.

Sawatzky, et al., 2013, Canada	N=200/ NP n=95 UC n=105	-Post-operative cardiac surgery/ -One site	- First coronary artery bypass surgery - Must have phone/ - 6 months -From discharge until 6 weeks	Outcomes of adult cardiac surgery follow-up model of care	-Telephone follow- up 3 days' post discharge. -Medical advice and/or education -Patient seen prn to manage care -Transitioned care to family physician by 6 weeks	-No difference Length of stay after cardiac surgery -No difference SF 36 physical and mental composite scores	-One cardiac surgery NP
Vernooij, et al., 2012, Greving, et al., 2015 The Netherlands	N=330/ NP n=164 UC n=166	-Vascular risk reduction/ -2 sites	-Coronary, cerebral, or peripheral artery atherosclerosis & at least 2 treatable risk factors not at target/ - 17 months/ - 1 year	-Internet based, NP-led adult outpatient vascular risk factor management program promoting self-management on top of usual care is more effective	-On top of usual care. -NP counseling via internet -followed Dutch cardiovascular risk management guidelines -supervised by internists	-Blinded outcomes -Decreased adjusted Framingham Risk score. ->#'s Reached LDL target & stopped smoking, - trend improvement in BMI, triglyceride levels & systolic blood pressure	- Nine NPs

NP=NP-led care
UC= usual care (Specific study: Blum – physician-led, Goldie – hospitalist-led, Rood- retrospective chart review, Sawatzky – physician-led, and Vernooij,- physician-led)

Figure 3.2: Risk of Bias Graph

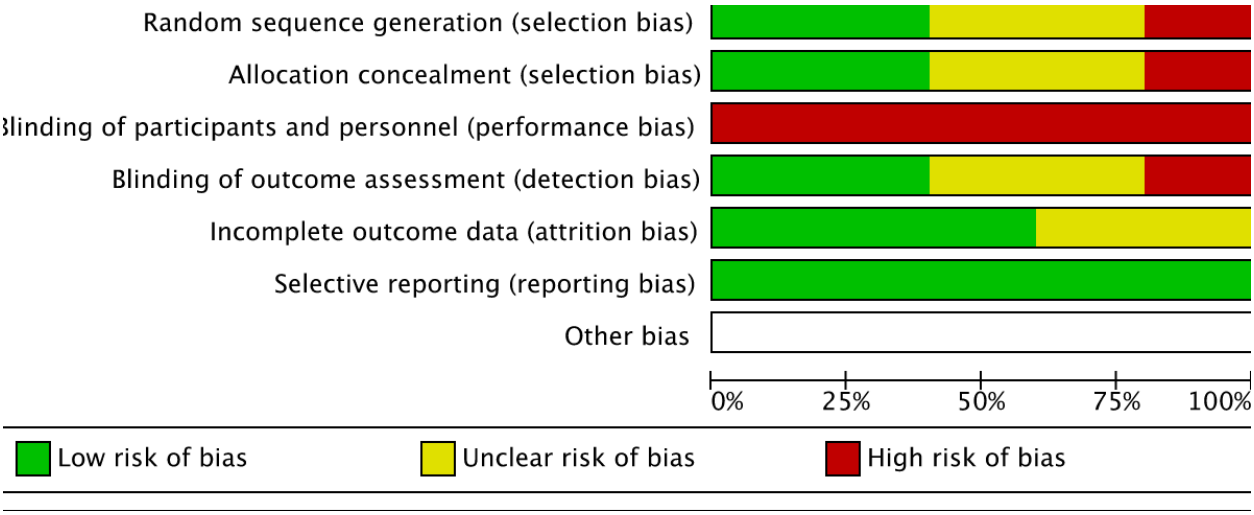


Figure 3.3: Risk of Bias Summary

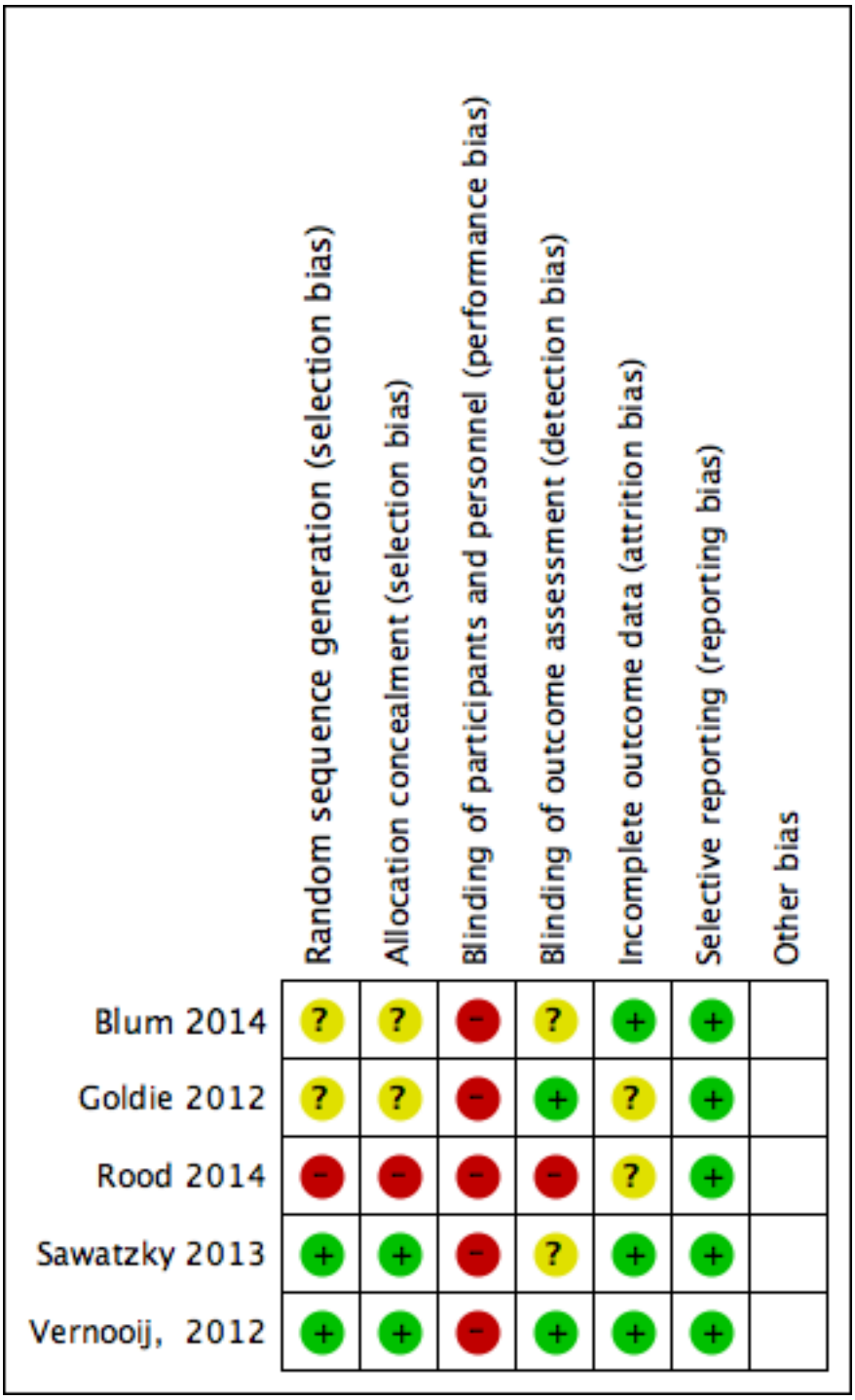


Table 3.2: GRADE Evidence Profile: NP Effectiveness in Cardiovascular Care

Quality Assessment						Summary of Findings					
						# Patients			Absolute Risk		
Outcome/ # of RCT	Risk of Bias	Incon-sistency	In-directness	Imprecision	Publica-tion Bias	Usual Care	NP-led Care	Relative Risk(RR) Mean Difference(MD) Relative Change (RC) (95% CI)	Con-trol Risk [a]	Risk Diff-erence	Quality
30-day re-admission HF/ 2	Very serious: lack of blinding with random-ization and patient selection	No serious	No serious	No serious	Un-detected	123/292 ad-mission	91/274 ad-mission	RR 0.74 (0.47-1.17)	42/ 100[c]	Not Sig-nificant	⊕⊕OO Low
SF36 Physical Composite 2	Serious: random-ization issues & cannot control for confound-ers	No serious	No serious	No serious	Undetect ed	206	197	MD: 0.17 (-0.89-1.23)	22 to 38/ 100	Not Sig-nificant	⊕⊕⊕O Mod-erate
SF36 Mental Composite 2	Serious: random-ization issues, cannot	No serious	No serious	No serious	Un-detected	206	197	MD: 0.16 (-0.47--.78)	21 to 50 /100	Not Sig-nificant	⊕⊕⊕O Mod-erate

	control for confound-ers										
Length of Stay 2	No serious	No serious	No serious i	Serious: random-ization process unclear	Un-detected	160	112	MD: -0.89 (-2.44-0.66)	9 to 9.5/ 100	Not sig-nificant	⊕⊕⊕O Mod-erate
Change in Framing-ham Risk Score 1	No serious	No serious	Serious: using change of Framing-ham score as measure of vascular risk	No serious	Un-detected	159	155	RC -12% (-22%, 3%)[b]	13.2 / 100	Not Sig-nificant	⊕⊕⊕O Mod-erate

Abbreviations: GRADE, Grading of Recommendations Assessment, Development and Evaluation; RCT, randomized controlled trials; CI. Confidence interval; RR, risk ration;

[a] The control rate is based on the median control group risk across studies.

[b] At baseline Framingham risk score higher in NP led care group (16.1 (SD 10.6) vx 14.0 (10.5); therefore adjusted for the separate variables of the Framingham risk score and for baseline Framingham heart risk score – producing a relative change as noted

[c] The control rate is based on the median control group risk across studies.

Figure 3.4: 30-Day Readmission Rate for Heart Failure

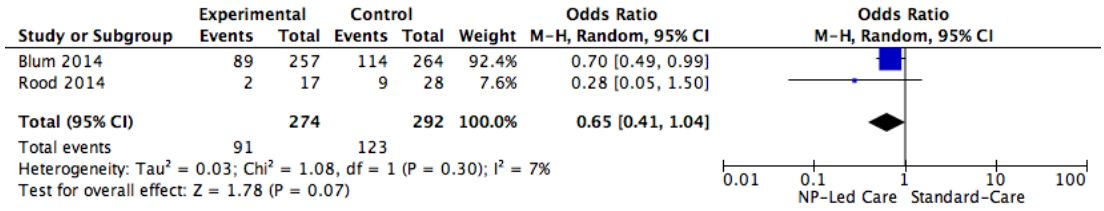


Figure 3.5: Length of Stay after Cardiac Surgery

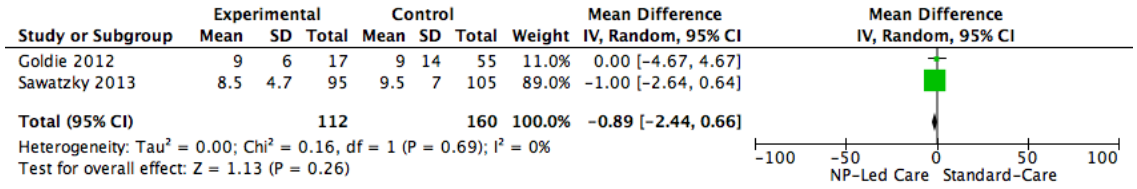


Figure 3.6: Health Related Quality of Life: SF36 Physical Composite Scores

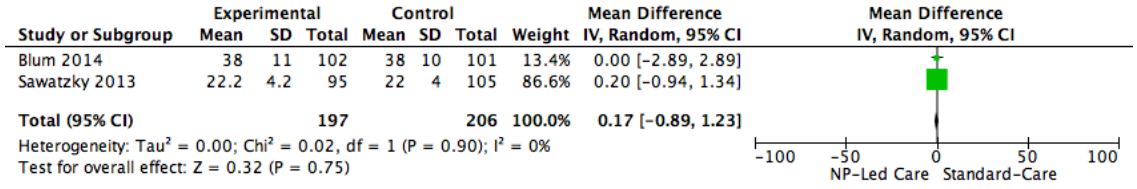
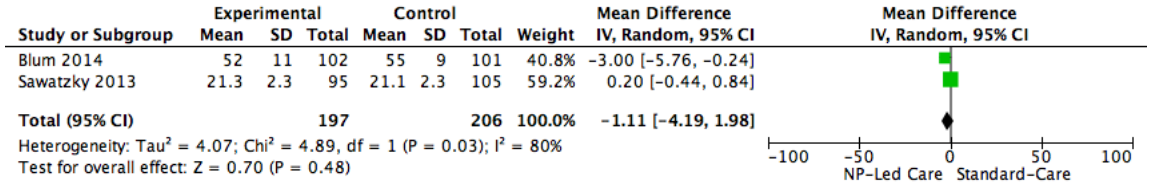


Figure 3.7: Health Related Quality of Life: SF 36 Mental Composite Scores



Chapter 4: The Effect of Nurse Practitioner-Led Care on Health-Related Quality of Life in Adult Patients with Atrial Fibrillation: Interim Results of a Randomized Controlled Trial

4.1 Introduction

The world healthcare crisis is fuelled by economic demands, population growth and the increasing prevalence of chronic diseases (1). It has been said Canada's healthcare system is in perennial crisis (2), with ongoing healthcare reform initiatives for the last forty years (3). Cardiovascular (CV) disease is one of the leading causes of death in Canada and the world (4). Atrial fibrillation (AF), the most common cardiac arrhythmia, is increasing in incidence and prevalence in Canada (5). It was estimated in 2010 that approximately 350,000 Canadians have AF (6). The risk of developing AF in patients over 40-years of age is one in four (7), and with our aging population, it is projected that the number of patients with AF will dramatically increase over the next decade (8). To meet this increasing patient care demand, new methods of care delivery are required.

Atrial fibrillation is associated with aging and chronic diseases such as hypertension and sleep apnea. While AF itself is not considered acutely life threatening, it is associated with devastating complications including stroke and heart failure (HF), which increase morbidity and healthcare costs. It is estimated that poorly controlled AF hospital visits cost the healthcare system $815 million per year (9). There is no cure for AF, therefore, treatment aims to decrease both symptoms and risk of complications and improve health related quality of life (HRQOL) (10). Currently, the first treatment strategy is to control the ventricular response rate of atrial fibrillation (11, 12). In 2002, the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial demonstrated no significant difference in mortality between

patients with AF who were rate controlled vs patients who were given rhythm-controlling medication (12). In fact, patients in the rhythm-control strategy had a higher incidence of torsade de pointes, cardiac arrest and hospitalization, compared to patients who were rate controlled. Given the AFFIRM trial results, the decision to progress therapy to rhythm-control is now guided by patients' symptoms and self-reported HRQOL.

Traditionally, patients with AF have their care provided by cardiologists, electrophysiologists and their primary care physician (13-15). Given the increased incidence and prevalence of AF, healthcare provider roles are being redeveloped or supported to work to full scope of practice, resulting in novel patient care delivery models (8, 13, 16, 17). In fact, clinical guidelines recommend the utilization of multidisciplinary teams (18). Nurse practitioners are registered nurses (RNs) with specialized graduate-level training enabling them to diagnose, order diagnostic testing, prescribe and provide treatment (19). They are independent healthcare providers who practice on a continuum including both independent and/or collaborative environments. To date, the effect of NP-led care on patients self-reported HRQOL, and patient satisfaction is unknown in patients with AF.

Comparing NP-led care with physician-led care in other populations, patients generally achieve similar health outcomes (20-22), and are more satisfied with NP-led care (20, 23, 24). Nurse practitioner-led care has also been shown to meet healthcare reform initiatives, by decreasing wait times, lengths of stay and healthcare costs (22, 25). Despite these positive benefits, there continues to be barriers to implementing the NP role (26, 27).

As the number of AF patients increase, new models of care are being trialed to try to meet patient needs. However, a review of the literature identified only one randomized

controlled trial (RCT) comparing RN-led care vs physician-led care for patients with AF (28). This study was completed at an outpatient clinic of a Dutch hospital, where AF patients were followed for 2 years. Registered Nurse-led care was guided by AF-specific decision support software. Patients were reviewed by the cardiologist at the end of the visit. The primary endpoint, a composite of cardiovascular hospitalization and cardiovascular death, occurred in 14.3% in the RN-led care group compared with 20.8% in the usual care group (HR 0.65, 95% CI 0.45–0.93, p = 0.017). Cardiovascular death occurred in 1.1% of the RN-led care group vs. 3.9% in the usual care group (HR 0.28, 95% CI 0.09–0.85, p = 0.025). Cardiovascular hospitalization occurred in the 13.5% in the RN-led care group vs. 19.1% in the usual care group (HR 0.66, 95% CI 0.46–0.96, p = 0.029). Registered nurse-led care had higher adherence to the AF clinical guidelines. Limitations for this study were that complex patients were excluded, and patient-reported outcomes such as HRQOL and patient satisfaction were not assessed. There are no RCTs for NP-led AF care, yet NPs have a much broader scope of practice, with the ability to work independently, which may provide more benefits to patient care and our strained healthcare system. Thus, the objective of this study was to assess the effect of NP-led care on HRQOL of adult patients with AF.

4.2 Methods

4.2.1 Study Design

The full study protocol has been previously published (29). Briefly, the present study is a prospective RCT comparing NP-led care to Standard care (cardiologist-led) of adult patients with AF referred to the Cardiac **E**nsuring **A**ccess and **S**peedy **E**valuation (EASE) clinic in a large tertiary care hospital in Alberta.

4.2.2 Study Population

All adult patients who were referred to the EASE clinic for assessment for AF were asked to participate in the study. Inclusion criteria comprised patients who were 18 years or older with documented AF who were able to provide informed consent and willing to complete the study questionnaires on their own or with assistance. Exclusion criteria were patients referred for AV node ablation or pulmonary vein isolation, patients who have failed rate control or antiarrhythmic medications, or have moderate to severe mitral or aortic valvular heart disease. Patients with unstable AF or who could not or were unwilling to attend follow up appointments were also excluded.

4.2.3 Randomization

Following verbal consent obtained during the telephone triage call, an RN randomized patients on a secure website. Blocked randomization (using variable block sizes) was used to ensure there were equal participants in the intervention and control groups and further concealed allocation. The patient was scheduled to attend the clinic they were randomized to within 4-6 weeks from the date of referral, consistent with Canadian Cardiovascular Society (CCS) guidelines(30)

4.2.4 Intervention and Control Groups

The intervention group received NP-led care. The initial visit was with an experienced CV NP with additional training in AF management. A complete baseline history and physical was completed to determine a plan of care based on current CCS AF Guidelines. $CHADS_2$/CHADSvasc score (31) were calculated to identify risk of stroke for each patient. CCS Severity of Atrial Fibrillation (SAF) scores (32) were completed to identify symptom severity of AF. If the patient developed HF, medication intolerances (which limited medical management), required assessment for treatment with amiodarone, electrical cardioversion or pulmonary vein isolation, or other serious complications, a cardiologist was consulted. The NP also provided

individualized patient education ("What is AF?", "AF management and complications"). The NP saw the patient in follow-up at three and six months as part of the intervention however, if the patient's condition required closer follow-up, timing was adjusted and documented.

The control group received standard care provided by a cardiologist in the EASE clinic. The cardiologist determined the AF management and follow up requirements as per their usual practice. The patient's care was referred back to the family physician if no follow-up was felt to be required.

4.2.5 Data Collection

Data collected at baseline and follow-up visits included the following:

- sociodemographic characteristics (gender, age);
- clinical physical findings (heart rate, rhythm on clinic ECG [sinus rhythm or AF], blood pressure, height and weight);
- CHADS-65;
- CHADSVASc;
- CCS AF score;
- type of AF (paroxysmal, persistent, permanent);
- symptoms (asymptomatic, anxiety, chest discomfort, HF, dizziness, fatigue, palpitations, presyncope, syncope, shortness of breath);
- clinical comorbidities [coronary artery disease (CAD), HF, hypertension, dyslipidemia, diabetes, thyroid disorders, renal insufficiency, chronic obstructive pulmonary disease, sleep apnea, stroke/TIA, tachymediated cardiomyopathy, smoking history, sedentary lifestyle, alcohol consumption, recreation drug use];
- echocardiogram findings (ejection fraction, atrial size);
- clinical intervention (ordered electrical cardioversion, ordered/changed rate or rhythm control, ordered/changed anticoagulation, weight loss, or stress counselling), testing ordered (echocardiogram, ischemia testing, rhythm monitoring); and
- referrals made (admission to hospital or referral to emergency from clinic, dietician, electrophysiologist, hypertension clinic, sleep apnea assessment).

Data were abstracted from the patients' electronic charts and Alberta NetCare (electronic provincial patient health information system) and entered into REDCap (Research Electronic Data Capture online database) by MJS.

Written questionnaires (Atrial Fibrillation Effect on Quality of life [AFEQT] & EQ-5D-3L) were collected in person, when written consent was obtained. Initially, all patient participants were mailed questionnaires to complete at three (AFEQT & EQ-5D-3L) and six months (AFEQT, EQ-5D-3L, and Consultant Satisfaction Questionnaire [CSQ]), with a return postage-paid envelope. As of January 2018, participants were offered the choice of completing the questionnaires online. All participants with outstanding questionnaires were contacted, regarding the option to change to the online method. Participants who had not completed written questionnaires were given two reminder phone calls. Online questionnaire non-responders were sent two reminder emails. In addition, at follow-up appointments, questionnaires were completed, if needed. Written questionnaires were entered into REDCap by MJS. Participants who answered the questionnaires online were emailed unique codes, specific to them, to answer the questionnaires directly into REDCap.

4.2.6 Measures

AFEQT is a AF-specific questionnaire (33) with 20 questions based on a 7-point Likert scale covering three domains. Four questions assess AF-related symptoms, eight questions evaluate daily function, and six questions evaluate AF treatment concerns. Two questions assess satisfaction with treatment and are not included in the overall score. A score of zero corresponds to complete disability/satisfaction, whereas as score of 100 corresponds to no disability or complete satisfaction.

The EQ-5D-3L is a simple, well-validated five question general quality of life (QOL) questionnaire (34). It assesses five dimensions of QOL: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The combined dimension scores create a Health Profile. The EQ-5D-3L also includes a visual analogue scale (VAS) on which patients' self-rate their

overall health. Zero is a worst imaginable health and 100 is the best imaginable health. It can also be transformed to a societal-based utility score (35) called EQ Index state. This score can be used to produce other outcomes such as Quality Adjusted Life Years (36). For this study we used Canadian value sets (TTO) to convert the ED-5D- 3L health state to an Index score.

The CSQ measures overall consultation satisfaction with the healthcare provider. It is a self-administered tool with 18 questions using a 5-point Likert scale, ranging from strongly agree to strongly disagree(37). Three factors are considered: professional aspects of the consultation, depth of patient relationship and perceived length of consultation. There are three questions related to overall general satisfaction. Scores range from zero to 100 with lower score associated with greater dissatisfaction and higher score with greater satisfaction.

4.2.7 Outcomes

The primary outcome was the difference in change between the NP-led care and Standard care groups in AFEQT scores from baseline to six months. Secondary outcomes include: 1) difference in EQ-5D-3L from baseline to six months between NP-led care and Standard care; 2) difference between NP-led care and Standard care groups in outcomes of death from cardiovascular causes, cardiovascular hospitalization, and emergency room visits (for ischemic stroke, HF, acute myocardial infarction, systemic embolism, major bleeding, severe arrhythmic events and life threatening adverse drug reactions); and 3) differences between the NP-led and Standard care groups in patient reported satisfaction with the consultation as measured by the Consultant Satisfaction Questionnaire(37).

4.2.8 Sample Size

A sample size of n=64 participants per group was calculated to detect a meaningful important difference (MID) of 12 in the overall AFEQT scores (SD 20, two-tailed t-test, 80%

power and α=5%)(29). Seventy participants per group (total n=140) allows for 10% loss to follow-up.

4.3 Results

4.3.1 Baseline Characteristics

Eighty-one patients were enrolled between July 23, 2016 and November 22, 2018. All patients attended their initial appointment and completed the baseline questionnaires (including the AFEQT and EQ-5D-3L) (NP-led n=41, Standard care n=40). Baseline characteristics and comorbidities appear to be similar between groups (Table 4.1). Average age was slightly lower in the NP-led group (62.52±12.79 vs 66.64±11.21) with fewer males (22±53.55 vs 25±62.50). Compared to the Standard care group, patients in the NP-led group were more likely to be in sinus rhythm (63% vs 53%) with paroxysmal AF (60% vs 48%) on rate control (93% vs 82%) at the initial clinic visit. In addition, a larger percentage had a history of hypothyroidism (17% vs 7.5%) and drank alcohol regularly (56% vs 17%). Patients in the NP-led group more commonly have a CHADS 65 score = 0 (39% vs 23%) but were less likely to have CHADS 65 score =1 (32% vs 43%). The cardiac ejection fraction (from the echocardiogram) was normal in both groups (57.85±8.71 vs 54.61±8.41), and both groups had the same percentage of patients with normal left atrial size (61% vs 61%).

With regards to reported symptoms, patients in the NP-led group tended to be more anxious (37% vs 18%), experienced dizziness (41% vs 23%), had more palpitations (56% vs 43%) and shortness of breath (32% vs 20%) compared to the Standard care group (Table 4.4). CCS SAF score of 2 was noted more often in the NP-led patients (25% vs 13%).

4.3.2 Baseline Participant HRQOL within Groups

Table 4.5 outlines participants' responses from the baseline AFEQT questionnaire. The NP-led group rated themselves with a higher overall AFEQT score (68.01±22.80 vs

61.18±23.97). However, patients in the NP-led group reported lower satisfaction with treatment (60.71±27.38 vs 67.08±24.53). EQ-5D-3L scores are reported in Tables 4.7 and 4.8. Patients in the NP-led group more frequently self-rated themselves as having no mobility issues (68% vs 64%), no problems with Self Care (98% vs 90%), or Usual Activities (68% vs 62%). Pain/Discomfort was rated as "none" by more patients in the NP-led group (61% vs 46%) however, more patients in the NP-led group self-reported moderate Anxiety/Depression (51% vs 33%). Patients in the NP-led group reported higher EQ VAS score (73.45±15.93 vs 65.78±19.38) and EQ Index scores (0.66 ±0.31 vs 0.60±0.43) compared to the Standard care group.

4.3.3 Baseline Therapies

At the initial consultation, patients in the NP-led care group had more rate control medication (41% vs 35%) and anticoagulation therapy (34% vs 15%) adjusted more often (Table 4.1). The NP-led care group also more received counselling for exercise (24% vs 0 %) and stress management (12% vs 0%). The NP-led group had more ischemia testing ordered (20% vs 5%) and rhythm monitoring (32% vs 0%) and more referrals to the dietician (5% vs 0%).

4.3.4 Follow-Up Characteristics

More patients in the NP-led care group attended three month (83% vs 14%) and six-month (88% vs 31%) follow up appointments, compared to Standard care. Response rates for follow up questionnaires appears to be similar between groups at three months (90% vs 100%), however six-month responses were greater in the NP-led arm (96% vs 77%).

Table 4.2 includes the three-month characteristics and clinical variables between the NP-led and Standard care group. Six-month characteristics and clinical variables are indicated in Table 4.3. At three months, patients who attended clinic follow up in the NP-led group were

more likely to be in AF (39% vs 20%) at the clinic appointment, have paroxysmal AF (50% vs 0%), and be on rate control medications (96% vs 40%). At six months, patients in the NP-led group were more likely to be in sinus rhythm (65% vs 50%) at the clinic appointment, experience paroxysmal atrial fibrillation (43% vs 38%) and were treated with rate control medications (78% vs 75%). Patients in the NP-led group at three months appear to be more likely to have a CHADS 65 score 0 (32% vs 30%) while at six months, a CHADS 65 score of 2 (25% vs 11%).

At the three month follow-up appointment, the NP-led group patients reported more palpitations (43% vs 20%), feelings of anxiety (28% vs 20%) and had a CCS AF score of 0 (32% vs 20%), compared to Standard care. At six months, patients in the NP-led group were more commonly asymptomatic (48% vs 25%) and a CCS AF score of zero (52% vs 25%).

4.3.5. Follow-Up Participant HRQOL Within Groups

Overall AFEQT scores within NP-led care increased slightly at three months and again at six months (76.52±18.88 to 80.84± 20.03) (Table 4.5). Within Standard care, the overall AFEQT scores initially increased at three months (76.22±22.32) but decreased slightly at six months (73.41±24.33). AFEQT symptom scores within the NP-led care group were also slightly higher at three months (84.38±17.60) and continued to increase at 6 months (88.14±14.42) while within the Standard care group, the symptom scores increased at three months (81.25±23.64) and decreased at six months (74.60±29.10). Treatment satisfaction scores within NP-led care continually increased from baseline to six months (73.84± 20.62 to 80.13± 20.83). Within the Standard care group, the treatment satisfaction scores increased at three months (71.13±25.20) but stayed essentially the same at six months (71.83±27.06).

EQ-5D-3L health profiles at three months (Tables 4.7) within the NP-led group had a greater proportion of patients who self-rated themselves as no problem in Mobility (77%), no Pain/Discomfort (64%) and no Anxiety/Depression (69%). At six months, within the NP-led group, the same proportion of patients self-rated themselves as no Pain/Discomfort (64%), however fewer patients reported no Anxiety/Depression (64%) and no problems with Mobility (68%). Within the Standard care group, self-rated profiles at three months there was an increase in the proportion of respondents with no problem with Mobility (71%), no Pain (75%) and no Anxiety/Depression (71%). At 6 months within the Standard care group, the proportion of patients who rated no problem with Mobility increased (80%), the proportion of patients with no Pain/Discomfort stayed the same (75%) while the proportion of patients with no Anxiety/Depression decreased to 60%.

Self-rated EQ VAS scores (Table 4.7) within the NP-led care group at three months increased slightly (75.72$\pm$15.17) and stayed essentially the same at six months (76.32$\pm$14.72). Within Standard care however, the EQ VAS scores increased at three months (72.17$\pm$17.87) and increased again at six months (76.81$\pm$15.68).

Calculated EQ-5D-3L Index scores (Table 4.8) within NP-led Care increased at 3 months (0.72$\pm$0.31) and decreased slightly at 6 months (0.70$\pm$0.31). Within Standard care, the Index scores rose at 3 months (0.72$\pm$0.35) and stayed the same at six months (0.72$\pm$0.38).

4.3.6 Follow-Up Therapies

At the three-month follow up appointment, patients in the NP-led group were more likely to have had their rate control medication changed (18% vs 0%) and be referred to an electrophysiologist (22% vs 20%) (Table 4.2), compared to Standard care. At six months, patients were more likely to receive exercise (13% vs 0%) and weight loss counselling (6.45% vs

0%) in the NP-led group (Table 4.3) compared to Standard care. Rhythm monitoring was ordered more frequently in NP-led group (17% vs 0%).

4.3.7 Primary and Secondary Outcomes

4.3.7.1 AFEQT

The primary outcome is the difference in change between the intervention and control groups in AFEQT total scores from baseline to six months. The difference from baseline to six months in NP-led care was 9.79 (SD 19.26), while the difference in Standard care was 7.76 (SD 29.25) (Table 4.6). The difference in change in AFEQT Overall scores between groups (NP-led and Standard care) was 2.03 (Figure 4.1).

4.3.7.2 EQ-5D-3L

The difference in change in EQ VAS Score from baseline to six months between NP-led care and Standard care (secondary outcome) was a change of 0.10 points. The calculated EQ Index score difference in change of scores from baseline to six months between NP-led care and Standard care was 0.08 points.

4.3.7.3 Cardiovascular Outcomes and CSQ

Secondary outcomes also included differences in composite cardiovascular outcomes. The electronic chart and NetCare were assessed retrospectively from date of enrollment until November 22, 2018. The outcomes were adjudicated by a blinded assessor. There was no difference in the outcome of death from cardiovascular causes (n=0 in both groups). Patients in the NP-led group had fewer hospitalizations (2.5% vs 10%) and emergency room visits (20% vs 28%) compared to the Standard care group (Table 4.9).

Difference in CSQ scores between NP-led care and Standard care at six months is presented in Table 4.10. The NP-led group reported higher satisfaction scores compared to the Standard care group (75$\pm$17.48 vs 71.25$\pm$13.10). Professional care (74.59 $\pm$12.22 vs

66.96±14.61) and Depth of Relationship (57.88±6.67 vs 55.25+7.34). Patients in the NP-led group rated perceived time (spent with the practitioner) as higher (38.78±12.90 vs 11.97±41.67) compared to the Standard care group.

4.4 Discussion

4.4.1 Main Findings

In this interim analysis of NP-led care compared to Standard care in patients with AF, patients in the NP-led Care group showed a slightly greater improvement of AF quality of life at 6 months. This difference of about 2 points is smaller than the minimally clinically important difference of 12. We anticipate that further insights into HRQOL subscales will emerge as the study continues to the full sample size.

When the sample size was initially determined for this study, MCID for change in AFEQT scores was thought to be 12 units (38). However, since then research has been completed to identify an estimate for a meaningful change in the AFEQT score. Since then, it has been suggested the MCID is most likely between six and 19 units (39). In our interim analysis, we observed a difference of only 2.03 units. However, we did observe a trend in improving AFEQT symptom scores in the NP-led group at three and six months, which indicates that patients are perceiving an improvement in their symptoms. Patient self-reported symptomatology at clinic visits also decreased at three and six months in the NP-led group.

Not surprisingly, there was no improvement in our generic quality of life measure, the EQ-5D-3L. It is known that generic HRQOL instruments do not focus on the specific effects of the disease and thus are less sensitive to detect clinically important differences in treatment effects (40).

Patient satisfaction scores were measured with the CSQ (four dimensions) and the AFEQT patient-rated Treatment Satisfaction score. All dimensions of the CSQ appear to be higher in the NP-led care group compared to the Standard care group. The dimension that appears to show the greatest difference between the groups was the Professional Care domain. The questions contributing to this score were related to clinic interactions, including the patient's perception of the physical exam and communication with the consultant. Perceived Time seems to have had the lowest score in each domain. Nurse Practitioner-led care appears to be rated higher than Standard care, however the scores were associated with a level of dissatisfaction. The questions contributing to this dimension were all negatively worded, which may have led to misunderstanding and, therefore participants may have inadvertently selected an answer which was incongruent with what they thought they were selecting (41). The AFEQT Treatment Satisfaction score is a separate domain, not included in the overall AFEQT score. In the NP-led group patient reported Treatment Satisfaction scores suggest a trend of improvement from baseline to six months. Standard care scores demonstrate an improvement in Treatment Satisfaction at three months, however at six months there is essentially no change.

The final outcome addressed differences in outcomes of death from a cardiovascular cause, cardiovascular hospitalization and emergency visits between groups. No deaths appear to have been reported to date in either group. In the NP-led group, one patient was hospitalized with a gastrointestinal (GI) bleed. The Standard care group also had one patient admitted for a GI bleed, one patient was admitted after pulmonary vein isolation, and two patients were admitted for AF. Identified emergency room visits for the NP-led group included two visits for bleeding concerns, and six for episodes of AF. In the Standard care group, it appears there were eight visits for AF, one for bleeding concerns, one for acute pulmonary embolism, and one for ischemic stroke. There

were appears to be a similar number of patients admitted for cardiovascular causes and emergency room visits between groups.

4.4.2 Previous Studies

As noted earlier, it was not possible to identify an NP-led care RCT in this patient setting. The RCT conducted in a Dutch hospital utilizing RN-led care for patients with AF, identified that clinical guideline adherence was higher in the RN-led group but, more significantly, it was found to be superior to physician-led care with lower incidence of cardiovascular hospitalizations and cardiovascular mortality. However, RNs utilized a computer-generated algorithm to determine care requirements; patients still needed to be assessed by the cardiologist and complex cases were excluded. Nurse practitioners' scope of practice is different from that of an RN. Nurse practitioner scope of practice includes many medical skills (independent patient assessment and treatment decisions) thus, freeing up cardiologists' time. Nurse practitioners can also consult and refer independently to other healthcare providers as needed, to ensure pertinent patient healthcare needs are met. At this point in the interim analysis, it appears that NP-led care patients may have similar cardiovascular outcomes as those under Standard care (a cardiologist), but with the added benefits of improved self-rated patient satisfaction and HRQOL scores.

The findings in this study correlate with NP-led research in other areas of care. Sangster-Gormley, et al., (2015) completed a three-year mixed methods study (questionnaires and patient interviews) to identify satisfaction with NP-led care and behavioural changes made as a result of the consult. While this was study of NPs in primary care, results indicated patients were very satisfied with their care and made more lifestyle changes (24).

NP-led care compared to physician-led care was also compared in an Australian emergency room fast-track setting to evaluate quality of care. Three-hundred-and-twenty patients

presented to emergency were triaged to either NP-led or physician-led care. Patient satisfaction was evaluated with a self-administered questionnaire, rating their experiences and follow-up health status and adverse events. Patient satisfaction was slightly higher in the NP-led care group compared with physician-led care and overall health outcomes and adverse events were similar between groups at two-weeks.(42)

4.4.3 Limitations

An obvious limitation to this report is that it presents the results of an unplanned interim analysis. When this research was initially designed, no problems were foreseen with recruitment, as the number of patients in the EASE clinic in previous years suggested that the study could be completed within two years. The clinic has experienced a decrease in the number of referrals since 2017. Additionally, the clinic encountered an RN shortage from January to July 2017, during which time recruitment was halted. As this study is part of MJS's thesis, a decision was made to perform an interim analysis.

Completing an unplanned interim analysis has implications for interpretation of the analysis. Typically, it exaggerates the treatment differences (43). Planned interim analysis should follow strict protocols, as the title suggests, they are preplanned during the design stage before enrolment in the study begins. Unplanned interim analysis can be completed however, only in acceptable instances, such as if there is an ethical reason to stop the study early (e.g., life threatening adverse events), when data from the two arms of the trial do not differ significantly (futile to proceed), and when there is very slow enrolment (44). While this trial has been slow to enroll, it was not the main impetus to perform an interim analysis. The main impetus was for the completion of MJS's doctoral studies.

One concern about performing an interim analysis is that the more times the data are assessed, the chances of achieving spurious statistical significance at the p=0.05 level

progressively increases (45). We do not plan to assess the data again until study completion. As this interim analysis is part of MJS's thesis, we did not include p values. There are also some variables with very few entries in one group and none in the other group, making it inappropriate to perform statistical testing. It seemed more appropriate to describe the data (e.g., the number of patients with the variable).

With the study being slow to recruit, this analysis also has small sample sizes. Sample size calculations have determined the need for 70 patients in each group, however, in this interim analysis, slightly more than half of the required sample is included. With a decreased sample size there is an increased risk of Type II error (decreased ability to detect a true difference) (46, 47). This must also be considered when analysing and interpreting the findings.

The Cardiac EASE Clinic receives AF referrals from general practitioners and emergency departments located in urban and rural areas. However, patients with AF are also cared for by family physicians and are referred to other cardiologists and AF clinics. Another limitation of this study is the possibility that participants received AF care from a provider not affiliated with the EASE Clinic (i.e., co-intervention). There is currently no way to monitor or determine other follow up care the patient may have received, which could have an impact on the outcomes being investigated in this trial (although patients in both groups presumably had equal access to their family physician).

Nurse practitioner education programs are typically generalist in nature and provide basic education regarding AF management (48). The PI (MJS) in this study is an NP with extensive clinical experience in cardiology and mentoring by AF specialists. An NP without the same experience and education may need additional mentoring to provide similar care.

4.4.4 Strengths

Strengths of this RCT include high questionnaire completion rates in both groups, and high follow-up rates in the NP-led group. Written consent and completed baseline questionnaires were received at the same time from all patients (100%) involved in this study. The follow-up questionnaires were either mailed to patients, completed on-line or completed in person at follow-up appointments. Follow-up appointments were discussed and, where relevant, booked at the baseline appointment.

4.4.5 Implications for Practice

In-person clinic follow-up appointments were scheduled at three and six months in the NP-led group as part of the intervention. Current clinical guidelines do not dictate or guide when and if follow-up appointments should be completed. Thus, follow-up in the Standard care group was left up to the individual practitioner. However, best practice suggests that if changes are made to medications or treatment, patients should be reassessed to see if the changes are effective and tolerated(49).

Previous studies suggested patients with AF tend to have a higher incidence of anxiety and depression (50). Assessing anxiety levels in clinic is just as important as assessing vital signs because of the potential impact it can have on how patients identify with their diagnosis and can affect patients' response to treatments (50). Strategies to help patients reduce their symptoms of anxiety include patient education and aggressive management of symptoms (50).

Patients are reporting high levels of anxiety in this study as preliminary results suggest 37% of patients in the NP-led group and 18% in the Standard care group self-reported anxiety at baseline. As well, 56% of patients self-reported experiencing Anxiety/Depression in the NP-led group and 43% in the Standard care group on the EQ-5D-3L (health dimension).

The NP-led group had extensive individualized patient education provided at the baseline visit and reinforced at each follow-up visit. Direct comparison of follow up results in self-reported symptoms is difficult as the Standard care group had fewer patients seen at follow-up appointments. However AFEQT symptoms scores includes assessment for anxiety and showed improvement consistently in the NP-led care group from baseline to six months.

These early findings suggest education and scheduled follow-up appointments provided within NP-led care based on the Shuler Model, maybe be associated with reducing anxiety in patients with AF and, thus, ultimately, improving response to treatment that promotes an increase in overall HRQOL.

4.4.6 Future Research

While the final study results are required to make definite interpretations and decisions regarding future research questions, some trends have already become apparent. As indicated earlier, patients with AF have a higher incidence of anxiety and depression, yet this is an area that to date has not been given much attention (51). Further investigation into how the timing and occurrence of follow-up appointments as well as whether NP-led care may have an effect on anxiety levels and therefore treatment outcomes of patients with AF, would be advantageous. Furthermore, healthcare resource allocation is very important. Ensuring cost-effectiveness and appropriate utilization of resources are essential in providing sustainable healthcare.

4.5 Conclusions

In this interim analysis of our randomized trial of NP-led care compared to Standard care, we found a small difference in AFEQT score of 2 units at 6 months of follow up. This trial is currently ongoing, with a projected end date of December 31, 2019. Completion of the study is imperative to have a true understanding of the effect of NP-led care on HRQOL in patients with

AF. Results will then be assessed for clinically meaningful differences between the models of care for patients with AF. The findings will help guide future practice and research.

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Table 4.1: Demographic, Clinical & Comorbid Variables by Treatment Groups at Baseline, Three & Six months

BASELINE		**Nurse Practitioner (n=41)**	**Standard care (n=40)**
Age:	mean (SD)	62.52 (12.79)	66.64 (11.21)
Gender: Male	n (%)	22 (53.66)	25 (62.50)
Height (cm):	mean (SD)	173.56 (10.38)	171.88 (11.00)
Weight (kg):	mean (SD)	93.62 (19.92)	93.90 (21.06)
Heart rate:	mean (SD)	71.37 (12.29)	76.40 (20.86)
Clinic ECG:	n (%)		
Atrial Fibrillation		15 (36.59)	18 (45)
Sinus rhythm		26 (63.41)	21 (52.50)
Blood Pressure:	mean(SD)		
Systolic		133.24 (10.79)	131.65 (17.84)
Diastolic		82.44 (10.31)	79.88 (10.85)
Type AF:	n (%)		
Paroxysmal		24 (60)	19 (47.50)
Persistent		10 (25)	15 (37.50)
Permanent		6 (15)	6 (15)
Control Strategy:	n (%)		
Rate		37 (92.50)	32 (82.05)
Rhythm		3 (7.5)	7 (17.95)
Co Morbidities:	n (%)		
CAD		1 (2.44%)	4 (10.00)
HF		2 (4.88)	2 (50.00)
Hypertension		20 (48.78)	22 (55.00)
DM		8 (19.51)	6 (15.00)
Hypothyroid		7 (17.07)	3 (7.50)
Creatinine Clearance	<50 ml/min	1 (2.44)	2 (5.00)
Sleep apnea		8 (19.51)	7 (17.50)
Stroke/TIA		2(4.88)	4 (10.00)
Sedentary		13 (31.71)	10 (25.00)
Tachymediated cardiomyopathy		1 (2.44)	3 (7.50)
Current Smoker		6 (14.63)	5 (12.50)
Ex-smoker (>5yrs)		18 (43.90)	13 (32.50)
Alcohol consumption		23 (56.10)	7 (17.10)
Recreational Drugs		1 (2.44)	2 (5.00)
CHADS 65:	mean (SD)	1.0 (1.02)	1.4 (1.26)
0		16 (39.02)	9 (22.50)
1		13 (31.71)	17 (42.50)
2		9 (421.95)	8 (20.00)
3		2 (4.88)	2 (5.00)
4		1 (2.44)	3 (7.50)

5	0 (0)	1 (2.50)
CHADS2VASc: mean (SD)	1.90 (1.50)	2.20 (1.60)
0	11 (26.83)	7 (17.50)
1	4 (9.76)	6 (15.00)
2	13 (31.71)	12 (30.00)
3	5 (12.20)	7(17.50)
4	7 (17.07)	5 (12.50)
5	1 (2.44)	1 (2.50)
6	0 (0)	2 (5.00)
CHADS 65>1 on anticoagulation: n (%)	24 (80.0)	32 (96.97)
Ejection Fraction: mean (SD)	57.85 (8.71)	54.61 (8.41)
Left Atrial Size: n (%)		
Normal	25 (60.98)	23 (60.53)
Mild	8 (19.51)	10 (26.32)
Moderate	4 (9.76)	3 (5.26)
Severe	4 (9.76)	2 (5.26)
Treatment: n (%)		
Electrical cardioversions ordered	2 (4.88)	9 (22.50)
Changed rate control	17 (41.46)	14 (35.00)
Changed rhythm control	3 (7.32)	3 (7.50)
Changed anticoagulation	14 (34.15)	6 (15.38)
Weight loss counselling	5 (12.20)	1 (2.50)
Exercise teaching	10 (24.39)	0 (0.0)
Stress counselling	5 (12.20)	0 (0.0)
Testing Ordered: n (%)		
Ischemia testing	8 (19.51)	2 (5.0)
Rhythm monitoring	13 (31.71)	0 (0.0)
Referrals: n (%)		
Admission to hospital	0 (0)	0 (0)
Dietician	2 (4.88)	0 (0)
Electrophysiologist	6 (14.63)	3 (7.50)
Emergency	1 (2.44)	0 (0)
Hypertension clinic	1 (2.44)	0 (0)
Sleep apnea assessment	3 (7.32)	3 (7.50)

n= number with the variable

Table 4.2: Demographic, Clinical, Comorbid & Therapeutic Variables by Treatment Group at Three Months

Three Month Follow-Up		**Nurse Practitioner (n=28)**	**Standard care (n=5)**
Heart rate:	mean (SD)	73.0 (11.68)	61.20 (18.51)
Clinic ECG:	n (%)		
Atrial Fibrillation		11 (39.29)	1 (20.20)
Sinus rhythm		17 (60.71)	4 (80.0)
Blood Pressure:	mean (SD)		
Systolic		131.93 (18.74)	120.40 (9.21)
Diastolic		76.96 (10.13)	70.6 (7.47)
Type AF:	n (%)		
Paroxysmal		14 (50.0)	0 (0)
Persistent		6 (21.43)	4 (80.0)
Permanent		8 (28.57)	1 (20.0)
CHADS 65:	mean (SD)	1.03 (0.98)	1.12 (1.08)
0		10 (32.26)	10 (30.30)
1		13 (41.94)	15 (45.45)
2		6 (19.35)	3 (9.09)
3		2 (4.88)	4 (12.12)
4		1 (3.23)	1 (3.03)
CHADS2VASc:	**m**ean (SD)	2.03 (1.43)	1.89 (1.47)
0		6 (19.35)	7 (21.21)
1		4 (12.90)	7 (21.21)
2		10 (32.26)	8 (24.24)
3		7 (22.58)	7 (21.21)
4		2 (6.45)	3 (9.09)
5		2 (6.45)	0 (0)
6		0 (0)	1 (3.03)
CHADS 65>1 on anticoagulation:	n (%)	22 (88.0)	26 (100.0)
Control Strategy:	n (%)		
Rate		27 (96.43)	2 (40.0)
Rhythm		1 (3.57)	3 (60.0)
Treatment:	n (%)		
Electrical cardioversions ordered		2 (7.14)	0 (0)
Changed rate control		5 (17.86)	0 (0)
Changed rhythm control		0 (0)	1 (20.0)
Changed anticoagulation		2 (7.14)	2 (40.0)
Weight loss counselling		2 (7.14)	0 (0)
Exercise teaching		4 (14.29)	0 (0)
Testing:	n (%)		
Ischemia testing		2 (7.14)	0 (0)
Rhythm monitoring		2 (7.14)	0 (0)
Referrals:	n (%)		

Admission to hospital	0 (0)	0 (0)
Electrophysiologist	6 (21.43)	1 (20.0)
Psychologist	2 (7.14)	0 (0)

n= number with the variable

Table 4.3: Demographic, Clinical, Comorbid & Therapeutic Variables by Treatment Groups at Six months

Six-Month Follow-Up	**Nurse Practitioner (n=23)**	**Standard care (n=8)**
Heart rate: mean (SD)	72.70 (13.28)	64.63 (11.34)
Clinic ECG: n (%)		
Atrial Fibrillation	8 (34.78)	4 (50)
Sinus rhythm	15 (65.32)	4 (50)
Blood Pressure: mean (SD)		
Systolic	129.74 (14.29)	129.0 (15.61)
Diastolic	77.26 (6.48)	72.38 (9.21)
Type AF : n (%)		
Paroxysmal	10 (43.48)	3 (37.50)
Persistent	5 (21.74)	2 (25.00)
Permanent	8 (34.78)	3 (37.50)
CHADS 65: **m**ean (SD)	1.21 (1.02)	1.0 (0.96)
0	6 (25.00)	9 (33.33)
1	10 (41.67)	12 (44.44)
2	6 (25.00)	3 (11.11)
3	1 (4.17)	3 (11.11)
4	1 (4.17)	0 (0)
CHADS2VASc: **m**ean (SD)	1.92 (1.56)	1.70 (1.49)
0	5 (20.83)	6 (22.22)
1	5 (20.83)	8 (29.63)
2	8 (33.33)	6 (22.22)
3	1 (4.17)	4 (14.81)
4	3 (12.50)	2 (7.41)
5	2 (8.33)	0 (0)
6	0 (0)	1 (3.70)
CHADS 65>1: on anticoagulation: n (%)	18 (94.74)	20 (95.24)
Control Strategy: n (%)		
Rate	18 (78.26)	6 (75.00)
Rhythm	5 (21.74)	2 (25.00)
Treatment: n (%)		
Changed rate control	0	3 (9.68)
Changed rhythm control	0	2 (25.00)
Changed anticoagulation	1 (4.35)	0 (0)
Weight loss counselling	2 (6.45)	0 (0)
Exercise teaching	3 (13.04)	0 (0)
Testing: n (%)		
Rhythm monitoring	4 (17.39)	0 (0)
Referrals: n (%)		
Admission to hospital	0 (0)	0 (0)
Dietician	1 (4.35)	0 (0)

Electrophysiologist	5 (21.74)	2 (25.0)

n= number with the variable

Table 4.4: Patient Symptoms: Self-Reported & CCS AF Score by Treatment Group at Baseline, Three and Six months

	Nurse Practitioner (n=41)	**Standard care (n=40)**
Baseline n (%)		
Symptom:		
Asymptomatic	10 (24.39)	14 (35.00)
Anxiety	15 (36.59)	7 (17.50)
Chest discomfort	8 (19.51)	3 (7.50)
HF symptoms	0 (0)	2 (5.00)
Dizzy	17 (41.46)	9 (22.50)
Fatigue	13 (31.71)	8 (20.00)
Palpitations	23 (56.10)	17 (42.50)
Presyncope	8 (19.51)	5 (12.50)
SOB	13 (31.71)	8 (20.00)
CCS AF Score:		
0	11 (26.83)	9 (22.50)
1	19 (46.34)	25 (62.50)
2	10 (24.39)	5 (12.50)
3	1 (2.44)	1 (2.50)
Three Month Follow-Up	**Nurse Practitioner (n=28)**	**Standard care (n=5)**
Symptom:		
Asymptomatic	9 (32.14)	1 (20.0)
Anxiety	8 (28.57)	1 (20.00)
HF Symptoms	1 (3.57)	1 (20.00)
Dizzy	6 (21.43)	4 (80.00)
Fatigue	9 (32.14)	3 (60.00)
Palpitations	12 (42.86)	1 (20.00)
Presyncope	2 (7.14)	2 (40.00)
Syncope	1 (3.57)	0 (0)
SOB	4 (14.29)	0 (0)
CCS AF Score:		
0	9 (32.14)	1 (20.00)
1	14 (50.00)	4 (80.00)
2	5 (17.86)	0 (0)
Six month Follow-Up	**Nurse Practitioner (n= 23)**	**Standard care (n=8)**
Symptom:		
Asymptomatic	11 (47.83)	2 (25.00)
Anxiety	3 (13.04)	0 (0)
Chest Discomfort	2 (8.70)	1 (12.50)
Dizzy	4 (17.39)	2 (25.00)
Fatigue	4 (17.39)	4 (17.39)

Palpitations	8 (34.78)	2 (25.00)
Presyncope	2 (8.70)	0 (0)
Syncope	1 (4.35)	1 (4.35)
SOB	4 (17.39)	3 (37.50)
CCS AF Score:		
0	12 (52.17)	2 (25.00)
1	10 (43.48)	4 (50.00)
2	0 (0)	2 (25.00)
3	1 (4.35)	0 (0)

n= number with the variable

Table 4.5: AFEQT Scores By Treatment Group at Baseline,
Three and Six Month Follow Up

AFEQT Scores Mean (SD)	NP	Cardiologist
Baseline	N=41	N=40
Overall Score	68.01(22.80)	61.18(23.97)
Symptoms	71.03(26.24)	67.50(28.81)
Daily Activities	67.11 (26.81)	58.91 (31.69)
Treatment Concerns	89.81(12.90))	86.39(13.52)
Treatment Satisfaction	69.71(27.81)	67.08(24.53)
3-Month	N=36	N=28
Overall Score	76.52 (18.88)	76.22(22.32)
Symptoms	84.38(17.60)	81.25(23.64)
Daily Activities	72.45(24.18)	73.69 (28.19)
Treatment Concerns	93.90 (12.06)	74.84(13.51)
Treatment Satisfaction	73.84 (20.62)	71.13 (25.20)
6-Month	N=26	N=20
Overall Score	80.84 (20.03)	73.41 (24.33)
Symptoms	88.14 (14.42)	74.60 (29.10)
Daily Activities	76.20(26.72)	74.70(23.98)
Treatment Concerns	97.44 (12.19)	93.39 (14.76)
Treatment Satisfaction	80.13 (20.83)	71.83 (27.06)

AFEQT scores – range 0-100.
A score of 0 corresponds with complete disability/no satisfaction
A score of 100 corresponds with no disability/complete satisfaction
MCID = 12 (Likely between 6-19 units); Significant improvement =19 unit

Table 4.6: AFEQT Scores at Baseline, Three and Six Months *as well as* Change Within Groups- Baseline to 6 months

AFEQT Domain	**Nurse Practitioner- Led Care**			**Δ Baseline to Six months**	**Standard care**			**Δ Baseline to Six months**
	Base line (n=42)	3-Mon (n=36)	6-Mon (n=26)	**Within NP-Led Care**	Baseline (n=40)	3-Months (n=28)	6-Month (n=31)	**Within Standard care**
Overall Score	68.01 (22.80)	76.52 (18.88)	80.84 (20.03)	**9.79 (19.26)**	61.18 (23.97)	76.22 (22.32)	73.41 (24.33)	**7.76 (29.25)**
Symptoms	71.03 (26.24)	84.38 (17.60)	88.14 (14.42)	**8.49 (18.73)**	67.50 (28.81)	81.25 (23.64)	74.60 (29.10)	**6.34 (34.10)**
Treatment satisfaction	60.71 (27.38)	73.84 (20.62)	80.13 (20.83)	**17.63 (33.44)**	67.08 (24.53)	71.13 (25.20)	71.83 (27.06)	**1.98 (18.23)**

AFEQT Scores: Difference in Change in AFEQT Scores Between Treatment Groups From Baseline to Six months
AFEQT Overall and Subscale Scores: score of 0 = complete disability; score of 100 = no disability
AFEQT Treatment Satisfaction Score: score of 0= no satisfaction; score of 100 = complete satisfaction
MID = 12 points (maybe between 6 -19points); Significant improvement in AFEQT score = 19 points
Δ = change in score

Figure 4.1 AFEQT Overall Scores by Treatment Group: Within Groups and Between Groups

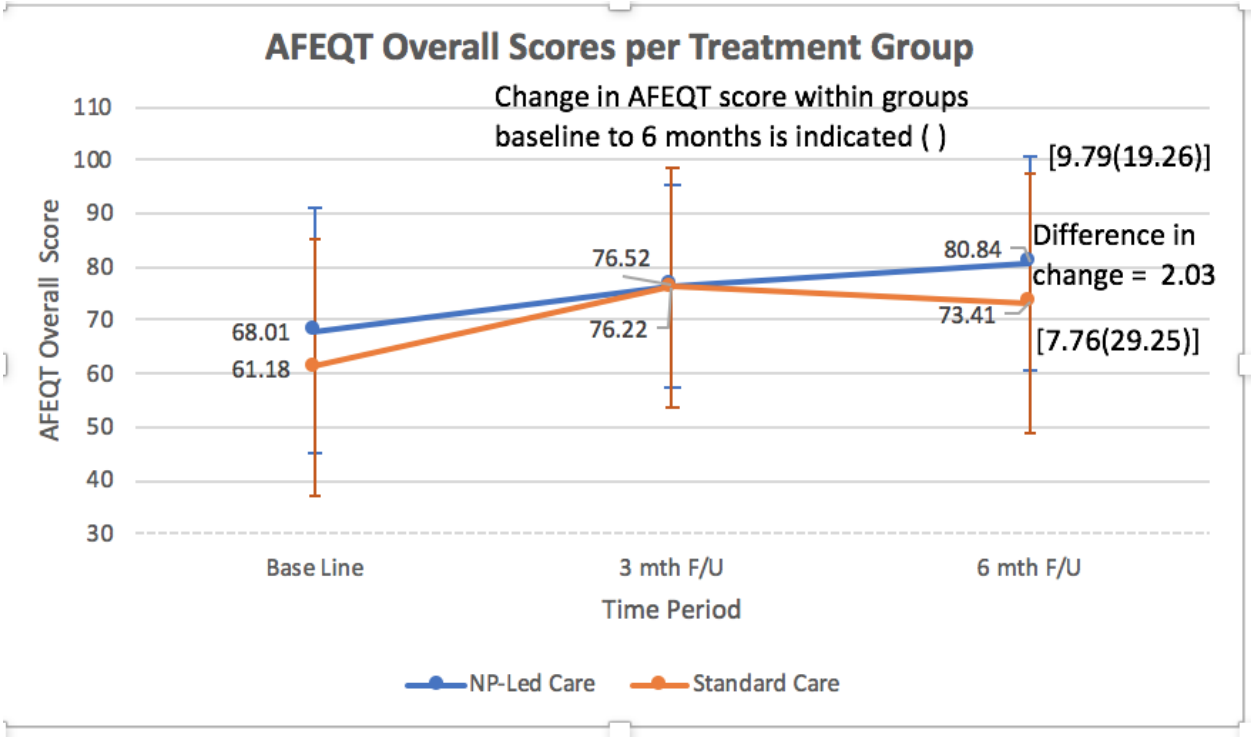

Table 4.7: EQ-5D-3L Scores by Treatment Group at Baseline, Three and Six months

EQ 5D 3L Scores	**Nurse Practitioner**	**Standard care**
Baseline	**n=42**	**n=40**
Mobility n (%)		
No problem	n=28 (68)	n=25 (64)
Some problems	n=13 (32)	n=14 (36)
Self-Care n (%)		
No problems	n=40 (98)	n=35 (90)
Some problems	n=1 (2)	n=4 (10)
Usual Activities n (%)		
No problems	n=28 (68)	n=24 (62)
Some problems	n=11 (27)	n=15 (39)
Unable to perform	n=2 (5)	n=0
Pain/Discomfort n (%)		
None	n=25 (61)	n=18 (46)
Moderate	n=15 (37)	n=18 (46)
Extreme	n=1 (2)	n=3 (8)
Anxiety/Depression n (%)		
None	n=18 (44)	n=22(56)
Moderate	n=21(51)	n=13 (33)
Extreme	n=2 (5)	n=4 (10)
EQ VAS Score: mean (SD)	73.45 (15.93)	65.78 (19.38)
Three Month Follow- Up	**n=44**	**n=42**
Mobility: n (%)		
No problem	n=27 (77)	n=20 (71)
Some problems	n=8 (23)	n=8 (29)
Self-Care: n (%)		
No problems	n=34(94)	n=26 (93)
Some problems	n=2 (6)	n=2 (7)
Usual Activities: n (%)		
No problems	n=26 (72)	n=18 (64)
Some problems	n=10 (28)	n=10 (36)
Pain/Discomfort: n (%)		
None	n=23 (64)	n=21 (75)
Moderate	n=11 (31)	n=5 (18)
Extreme	n=2 (6)	n=2 (7)
Anxiety/Depression: n (%)		
None	n=25 (69)	n=20 (71)
Moderate	n=11 (31)	n=7 (25)
Extreme	n=0	n=1 (4)
EQ VAS Score: mean (SD)	75.72 (15.17)	72.17 (17.87)

Six Month Follow-Up	**n=40**	**n=37**
Mobility: n (%)		
No problem	n=19 (68)	n=16 (80)
Some problems	n=9 (32)	n=4 (20)
Confined to bed		
Self-Care: n (%)		
No problems	n=26 (93)	n=20 (100)
Some problems	n=2 (7)	n=0
Usual Activities: n (%)		
No problems	n=20 (71)	n=12 (60)
Some problems	n=7 (25)	n=8 (40)
Unable to perform	n=1 (7)	n=0
Pain/Discomfort: n (%)		
None	n=18 (64)	n=15 (75)
Moderate	n=7 (25)	n=4 (20)
Extreme	n=3 (11)	n=1 (5)
Anxiety/Depression: n (%)		
None	n=18 (64)	n=12 (60)
Moderate	n=10 (36)	n=6 (30)
Extreme	n=0	n=2 (10)
EQ VAS Score: mean (SD)	76.31 (14.72)	76.81 (15.68)
Change Within Group: Baseline to Six Months	0.04 (0.03)	0.14(0.46)
Change Between Groups: Baseline to Six Months	0.10	

n= number with the variable

Health Profile (Dimension Scores))(self-reported):

1 = no problems; 2= some problems; 3= severe problems/unable to do

If the level is not indicated – no patients rated themselves at that level

EQ VAS Scores (self-reported perspective on their own health):

0 = worst imaginable health; 100 = best imaginable health

MCID: 7-10 points

Table 4.8: EQ-5D-3L Index Scores, Baseline, Three and Six Months

EQ5 D 3L Index score									
	Nurse Practitioner			**Change within NP Baseline to six months**	**Standard care**			**Change within Standard care Baseline to six months**	**Difference in change Between Groups Baseline – six months**
	Baseline (n = 44)	**3 Month** (n = 40)	**6 Month** (n = 31)		**Baseline** (n = 42)	**3 Month** (n = 37)	**6 Month** (n = 31)		
Score Mean (SD)	0.66 (0.31)	0.72 (0.31)	0.70 (0.31)	0.04	0.60 (0.43)	0.72 (0.35)	0.72 (0.38)	0.12	0.08

EQ-5D-3L Index Score of Health State (calculated – weighted by preferences of the general population):
Full health =1, dead =0
MCID= 0.03

Table 4.9: Cardiovascular Outcomes by Treatment Group

CV Variables	Nurse Practitioner n=41	Standard care n=40
Death	0	0
CV Hospitalizations n (%)	1 (2.5)	4 (10)
Reason	GI Bleed	Post PVI, AF (2) GI Bleed
Emergency Room Visits:	0	0
Ischemic stroke	0	1 (2.4)
Heart failure	0	0
Acute myocardial infarct	0	0
Systemic embolism	0	1(2.4)
Bleeding	2 (4.9)	1 (2.4)
Arrhythmic events	6 (14.63)	8 (20.00)
Adverse drug reactions	0	0

Table 4.10: Consultation Satisfaction Questionnaire Scores by Treatment Group at Six Month

CSQ Variables Mean (SD)	Nurse Practitioner (n=26)	Standard care (n=20)
General satisfaction	75.00 (17.48)	71.25 (13.10)
Professional care	74.59 (12.22)	66.96 (14.61)
Depth of relationship	57.88 (6.67)	55.25 (7.34)
Perceived time	38.78 (12.90)	11.97 (41.67)

CSQ scores: low scores:=greater dissatisfaction; high scores:=greater satisfaction
Range: 0-100

Chapter 5: Conclusion

5.1: Summary

Cardiovascular disease (CV) is the leading cause of death globally (1). Canada spends more than $20.9 billion every year on CV care (2). Healthcare reform has been ongoing over the last 40 years to try to curtail costs while ensuring that accessible, high quality healthcare is available to the population (3, 4). In 2010, there were 350,000 Canadians living with atrial fibrillation (AF) (5). This number is anticipated to rise exponentially because of Canada's aging population. With sustainability of the current healthcare system being strained (4, 6), new models of care are being considered to provide quality patient centered care. The new model of care we are proposing is utilizing nurse practitioner (NP)-led care to improve outcomes for patients with AF.

Nurse practitioners are highly skilled healthcare practitioners who work independently, but also work within collaborative teams (7). Their scope of practice includes advanced nursing skills as well as skills previously only associated with medicine. Nurse practitioner-led models of care have been associated with increased patient satisfaction, decreased wait times, greater patient adherence to treatment plans and improved patient-reported outcomes. Atrial fibrillation is a complex chronic disease associated with stroke and heart failure - both known to lead to increased mortality (8) as well as higher costs to the healthcare system (8). The Shuler Nurse Practitioner Model is a conceptual model utilized to guide NP-led Care for patients with AF. The model brings together the benefits of advanced nursing practice with select medical skills to provide patient-oriented holistic care to patients with AF. Patients become more empowered to learn and make effective changes to limit how AF affects their lives. Thus, utilizing NP-led care based on the Shuler Model could be an effective model of care to improve health outcomes including health-related quality of life (HRQOL) in patients living with AF.

The overarching theme of this thesis was to examine CV NP-led care and the associated outcomes of care in patients with AF. Two studies were undertaken. The first was a systematic review and meta-analysis to assess the evidence from randomized controlled trials (RCTs) on the impact of CV NP-led care. Five studies were found that met the inclusion criteria. The studies were assessed to have predominantly low to moderate-quality evidence for 5 CV NP-led outcomes of care. In these investigations, no statistical differences were identified between NP-led care and standard-care for 30-day readmissions for heart failure, HRQOL (SF 36 physical and mental composite scores) and length of stay after cardiac surgery. Cardiovascular NP-led care may be associated with a small beneficial effect on vascular risk.

The second study was an RCT to assess the effect of NP-led care on HRQOL in adult patients with AF (9). This study was initiated in July 2016. Currently, there are 81 patients enrolled. The projected end date for this study is December 31, 2019. However, the study will continue until sample size requirements have been met (70 patients in each group). An interim analysis has been completed for the purposes of MJS's thesis. The major findings from this analysis suggest that NP-led care is associated with a small difference in change (of about two units) in AF quality of life as measured by the overall AFEQT scores at six months. There was essentially no difference between NP-led and Standard care group in EQ-5D-3L Index scores at six-months. Composite CV outcomes of death from CV causes, CV hospitalization and emergency room visits appear to be similar between groups. Patient satisfaction appears higher in the NP-led group, as noted in the CSQ and AFEQT treatment satisfaction scores. Completion of the study, however, is essential to have a better understanding of the true benefits of NP-led care of patients with AF. Previous research has identified benefits of NP-led care in other settings. Nurse practitioner-led care has been found to improve patient satisfaction (10-12),

decrease mortality (13), improve adherence to guidelines (14), better patient compliance with prescribed treatments (10, 15), associated with improved or equivalent HRQOL (16, 17), and provide similar outcomes to physician-led care (17-19). Taken together, the trends found in the current study suggest some modest benefits of NP-led care in patients with AF.

5.2 Future Research

The results of the studies included in this thesis document suggest that NP-led care guided by the Shuler Nurse Practitioner Practice Model, has promise to help address some of the challenges identified by healthcare reform. However, the acute care NP role has been present in the hospital setting since the late 1980s. While the benefits of NP-led care have been known, there continues to be barriers to the successful implementation of the role (20). The CV NP-led systematic review identified there were few RCTs completed, mostly of low to moderate quality. Further high quality research is required to gain a better understanding of what the current barriers and enablers are, to improve the sustainability of the NP role.

Currently there is not a standardized method to develop CV NP training or identify CV NP expertise within Canada. This might limit the generalizability of our findings. In the United States several different approaches have been taken, such as a formal CV residency (21), a CV-NP specialty program (22) and a board certification CV NP Exam (23). The CV NP and academic community in Canada may need to discuss options for NPs to develop standardized CV knowledge and skills which would allow for recognition as a CV NP.

Patients with AF are known to have a higher incidence of anxiety, which can trigger AF. Early results of the RCT we are completing identified 37% of patients at baseline reported symptoms of anxiety in the NP-led group which decreased to 8% at three months and 3% at six months. This could be clinically important. There is limited research and knowledge in this area

to help patients relieve their anxiety (24). Patients with anxiety are known to have lower HRQOL (25), as anxiety affects how symptoms are perceived (24). Rationally speaking, if treatments are aimed at decreasing episodes of AF, it should follow that symptoms of anxiety would dissipate. However, the use of antiarrhythmics or ablation does not necessarily resolve anxiety (26). Further research is warranted to determine how best to assist patients to decrease their anxiety levels. Investigating non-pharmacological options could be beneficial, since many medications used for anxiety can prolong QT/QTC intervals, which can cause other arrhythmias. Recent research suggests patients who exercise and maintain their weight at recommended levels improves their burden of AF (27). However, can this also decrease anxiety? Future research into the effect of cardiac rehabilitation on anxiety symptoms in patients with AF may provide helpful insight.

Finally, the systematic review completed as part of this dissertation also identified that many research abstracts on NP-led care were not developed into published manuscripts. This in effect prevents the benefits of NP-led care from being translated into practice. Support and mentorship to NPs as clinician scientists must be provided to facilitate and ensure that research by and for NPs is available in the peer-reviewed literature. This will also help to underscore that all existing research is utilized to provide evidence for the safety and benefits of NP-led care.

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Appendix A

Electronic database search strategies for Outcomes of Care for CV NP-led Systematic Review

CINAHL with full text

((MH "Heart Diseases+") or cardio* or cardia* or heart* or coronary or angina* or ventric* or myocard* or pericard* or ischem* or ischaem* or emboli* or thrombo* or "atrial fibrillat*" or tachycard* or arrhythmi* or endocard* or "sick sinus" or hypertensi* or "peripheral artery disease*" or ((high or increased or elevated) w2 "blood pressure") or hyperlipid* or hyperlipemi* or hyperlipaemi* or hypercholester* or hyperlipoprotein* or hypertriglycerid* or cholesterol or "blood pressure") AND (...

Limit to RCT,, 2007-2017

Web of Science (cardio* or cardia* or heart* or coronary or angina* or ventric* or myocard* or pericard* or ischem* or ischaem* or emboli* or thrombo* or "atrial fibrillat*" or tachycard* or arrhythmi* or endocard* or "sick sinus" or hypertensi* or "peripheral artery disease*" or r hyperlipid* or hyperlipemi* or hyperlipaemi* or hypercholester* or hyperlipoprotein* or hypertriglycerid* or cholesterol or "blood pressure ") *AND* **TOPIC:** ("nurse practitioner*") *AND***TOPIC:** (random* or trial or groups or "quasi experimental")
Refined By: **PUBLICATION YEARS:** (2015 OR 2013 OR 2016 OR 2008 OR 2011 OR 2009 OR 2007 OR 2014 OR 2010 OR 2012 OR 2017)

Scopus TITLE-ABS-KEY (cardio* OR cardia* OR heart* OR coronary OR angina* OR ventric* OR myocard* OR pericard* OR ischem* OR ischaem* OR emboli* OR thrombo* OR "atrial fibrillat*" OR tachycard* OR arrhythmi* OR endocard* OR "sick sinus" OR hypertensi* OR "peripheral artery disease*" OR hyperlipid* OR hyperlipemi* OR hyperlipaemi* OR hypercholester* OR hyperlipoprotein* OR hypertriglycerid* OR cholesterol OR "blood pressure") AND TITLE-ABS-KEY ("nurse practitioner*") AND TITLE-ABS-KEY (random* OR trial OR groups) AND (LIMIT-TO (PUBYEAR , 2017) OR LIMIT-TO (PUBYEAR , 2016) OR LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMIT-TO (PUBYEAR , 2012) OR LIMIT-TO (PUBYEAR , 2011) OR LIMIT-TO (PUBYEAR , 2010) OR LIMIT-TO (PUBYEAR , 2009) OR LIMIT-TO (PUBYEAR , 2008) OR LIMIT-TO (PUBYEAR , 2007))

Ovid MEDLINE

1. exp heart defects, congenital/ or exp heart diseases/

2. (cardio* or cardia* or heart* or coronary or angina* or ventric* or myocard* or pericard* or isch?em* or emboli* or thrombo* or atrial fibrillat* or tachycard* or arrhythmi* or endocard* or sick sinus or hypertensi* or peripheral artery disease* or ((high or increased or elevated) adj2 blood pressure) or hyperlipid* or hyperlip?emi* or hypercholester* or hyperlipoprotein* or hypertriglycerid* or cholesterol or blood pressure).ti,ab,kf.

3. 1 or 2

4. Nurse practitioners/ or nurse practitioner*.ti,ab,kf.

5. 3 and 4

6. limit 5 to yr="2007 -Current"

7. randomized controlled trial.pt.

8. clinical trial.pt.

9. (randomi?ed or quasi experimental).ti,ab,kf.

10. placebo.ti,ab,kf.

11. dt.fs.

12. randomly.ti,ab,kf.

13. trial.ti,ab,kf.

14. groups.ti,ab,kf.

15. or/7-14

16. animals/

17. humans/

18. 16 not (16 and 17)

19. 15 not 18

20. 6 and 19

Ovid EMBASE

1. exp heart disease/

2. (cardio* or cardia* or heart* or coronary or angina* or ventric* or myocard* or pericard* or isch?em* or emboli* or thrombo* or atrial fibrillat* or tachycard* or arrhythmi* or endocard* or sick sinus or hypertensi* or peripheral artery disease* or ((high or increased or elevated) adj2 blood pressure) or hyperlipid* or hyperlip?emi* or hypercholester* or hyperlipoprotein* or hypertriglycerid* or cholesterol or blood pressure).ti,ab,kw.

3. 1 or 2

4. Nurse practitioners/ or nurse practitioner*.ti,ab,kw.

5. 3 and 4

6. exp clinical trial/

7. (randomi?ed or quasi experimental).ti,ab,kw.

8. placebo.ti,ab,kw.

9. dt.fs.

10. randomly.ti,ab,kw.

11. trial.ti,ab,kw.

12. groups.ti,ab,kw.

13. or/6-12

14. animal/

15. human/

16. 14 not (14 and 15)

17. 13 not 16

18. 5 and 17

19. limit 5 to randomized controlled trial

20. 18 or 19

21. limit 20 to yr="2007 –Current

Cochrane Library Database of Systematic Review and Controlled Trials (Ovid Central)

1. exp Cardiovascular Diseases/

2. (cardio* or cardia* or heart* or coronary or angina* or ventric* or myocard* or pericard* or isch?em* or emboli* or thrombo* or atrial fibrillat* or tachycard* or arrhythmi* or endocard* or sick sinus or hypertensi* or peripheral artery disease* or ((high or increased or elevated) adj2 blood pressure) or hyperlipid* or hyperlip?emi* or hypercholester* or hyperlipoprotein* or hypertriglycerid* or cholesterol or blood pressure or stroke* or stokes or cerebrovasc* or cerebral vascular or apoplexy or ((brain or cerebral or lacunar) adj2 (accident* or infarct*))).ti,ab,kw.

3. 1 or 2

4. Nurse practitioners/ or nurse practitioner*.ti,ab,kw.

5. 3 and 4

6. (Adolescent/ or exp Infant/ or exp Child/) not ((Adolescent/ or exp Infant/ or exp Child/) and (exp Adult/ or exp Aged/))

7. 5 not 6

8. limit 7 to yr="2007 –Current

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all(cardio* OR cardia* OR heart* OR coronary OR angina* OR ventric* OR myocard* OR pericard* OR ischem* OR ischaem* OR emboli* OR thrombo* OR “atrial fibrillat*” OR tachycard* OR arrhythmi* OR endocard* OR “sick sinus” OR hypertensi* OR “peripheral artery disease*” OR hyperlipid* OR hyperlipemi* OR hyperlipaemi* OR hypercholester* OR hyperlipoprotein* OR hypertriglycerid* OR cholesterol OR blood pressure”)AND all (“nurse practitioner*”) AND all(pd(20070101-20171231))