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**Behaviour change interventions to improve medication adherence inpatients with cardiac disease: Protocol for a mixed methods study including a pilot randomized controlled trial**

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## **Abstract**

**Background:** Suboptimal adherence to medication increases mortality and morbidity; individually tailored supportive interventions can improve patients' adherence to their medication regimens.

**Aims:** The study aims to use a pilot randomised controlled trial (RCT) to test the hypothesis that a theory-based, nurse-led, multi-faceted intervention comprising motivational interviewing techniques and text message reminders in addition to standard care will better promote medication adherence in cardiac patients compared to standard care alone. The pilot study will assess self-reported adherence or non-adherence to cardiovascular medication in patients referred to a cardiac rehabilitation program following hospital admission for an acute cardiac event and test the feasibility of the intervention. The study will examine the role of individual, behavioural and environmental factors in predicting medication non-adherence in patients with CVD.

**Methods:** This is a mixed-methods study including a nested pilot RCT. Twenty-eight cardiac patients will be recruited; an estimated sample of nine patients in each group will be required for the pilot RCT with 80% power to detect a moderate effect size at 5% significance, and assuming 50% loss to follow-up over the six month intervention. Participants will complete a paper-based survey (Phase one), followed by a brief semi-structured interview (Phase two) to identify their level of adherence to medication and determine factors predictive of non-adherence. Participants identified as 'non-adherent' will be eligible for the pilot randomised trial, where they will be randomly allocated to receive either the motivational interview plus text message reminders and standard care, or standard care alone.

**Discussion:** Nurse-led multi-faceted interventions have the potential to enhance adherence to cardiac medications. The results of this study may have relevance for cardiac patients in other settings, and for long-term medication users with other chronic diseases.

**Keywords:** Cardiac disease, medication adherence, pilot randomised controlled trial, motivational interviewing, text messaging, nursing.

## **Summary of Relevance**

### **Problem**

Cardiovascular disease remains one of the leading causes of morbidity and mortality in Australia and worldwide.

### **What is already known**

Adherence to cardiovascular medication is suboptimal, increasing the risk of mortality and morbidity.

### **What this paper adds**

This is the first multi-method pilot randomised controlled trial of an intervention comprising motivational interviewing techniques and text reminders delivered by nurses to promote adherence to medication. Outcomes will support the development of a full-scale trial of the intervention in cardiac rehabilitation and other health care areas, and to patients with other chronic conditions who take long-term medications.

## **Introduction**

World-wide, the prevalence of cardiovascular disease (CVD) is increasing rapidly because of changes in population lifestyles (Hauptman, 2008), resulting in major concerns for community health (Zhu, Wang, Zhu, Zhou, & Wang, 2015). Cardiovascular disease has emerged as a leading cause of death and disability in Australia (Nichols, Peterson, Alston, & Allender, 2014), affecting one in six people and responsible for 16% of the nations' total disease burden. It is the main reason for rehospitalisation (Australian Institute of Health and Welfare, 2014); costs in 2004-5 of AU\$5.94 billion accounted for 11% of Australia's total health expenditure (Australian Institute of Health and Welfare, 2010). Quality of life has been shown to improve for patients with CVD referred to a comprehensive cardiac rehabilitation and secondary prevention program (Shepherd & While, 2012). These programs comprise recovery and preventative activities aimed at modifying cardiac risk factors and enhancing physico-psycho-social function to reduce the risk of subsequent cardiac events (Woodruffe et al., 2014). Cardiac rehabilitation enables changes in patient lifestyles by providing education and development of skills to reduce cardiovascular risk factors, and to promote adherence to prescribed medications.

Prescription medications, an important form of secondary prevention for CVD, have been a key factor in the 20% reduction seen in mortality rates within one year of diagnosis of acute myocardial infarction (AMI) (Chase, Bogener, Ruppert, & Conn, 2016); and the 28% reduction within three months of AMI between 2006 and 2007 (Kolandaivelu, Leiden, Gara, & Bhatt, 2014). While cardiac medications have been shown to be effective for symptom management and slowing the progression of CVD, consistent adherence to prescribed medication regimes is required to achieve these effects (Hunt et al., 2009).

The World Health Organisation (WHO) defines adherence as 'the extent to which a person's behaviour (taking medications, following a recommended diet and/or executing lifestyle changes) corresponds with the agreed recommendations of a healthcare provider' (Sabaté, 2003, p. 3). Adherence to medications is a challenge, particularly for patients with cardiac disease who often require multiple medications for prolonged periods (World Health Organisation, 2003). The risk of mortality and morbidity in such patients increases if adherence to prescribed medication is suboptimal (Hope, Wu,

Tu, Young, & Murray, 2004); yet reported rates of non-adherence vary from 33% to more than 50% (Li, Kuo, Hwang, & Hsu, 2012; Munger, Van Tassell, & LaFleur, 2007; Shah, Desai, Gajjar, & Shah, 2013), contributing to increased numbers of CVD-related Emergency Department visits, hospitalisation, reduced health and well-being, augmented healthcare costs and risk of death (Mukhtar, Weinman, & Jackson, 2014; Whittle et al., 2016). It is therefore important to identify the factors that influence medication adherence (Munger et al., 2007) and provide tailored interventions to improve patients' medication-taking behaviours (Santo et al., 2016).

## **Background**

Medication adherence is linked to better clinical outcomes among patients with heart disease, reducing the risk of hospital readmission and death (Ruppar, Cooper, Mehr, Delgado, & Dunbar-Jacob, 2016). Suboptimal medication adherence is a multidimensional issue. Socio-economic and patient-related factors include low educational levels, inadequate knowledge about disease and medications, beliefs about medications and patients' motivation to manage their illness and improve their overall health (Broekmans, Dobbels, Milisen, Morlion, & Vanderschueren, 2010). Lack of social support and psychological, cognitive or medical vulnerability can also play a part (Kronish & Ye, 2013). Factors shown to predict medication non-adherence include low self-efficacy, attitudes and beliefs about medications, low perceived behavioural control, and lack of social support (Morrison et al., 2015). Patients with concerns about their medications are more likely to report forgetting to take them or intentionally skipping doses (World Health Organisation, 2003). Older people and people in poor health or with co-morbidities are less likely to successfully self-administer (Krueger et al., 2015). Medication self-efficacy and beliefs about medications may also influence the adoption and maintenance of medication adherence behaviours (Bane, Hughe, & McElnay, 2006), and these factors can be affected by psycho-social factors such as the perceived level of social support and mood (Cha, Erlen, Kim, Sereika, & Caruthers, 2008).

Exploring patients' emotions and beliefs while helping to strengthen their self-efficacy may minimise barriers to behavioural change and motivate them to adhere to their medications (Riegel, Masterson Creber, Hill, Chittams, & Hoke, 2016). It is important to promote behavioural change by

exploring what drives an individual patient to make changes or to maintain the status quo. This can be achieved by applying motivational interviewing techniques that have been found to be effective in assessing a patient's readiness to change and subsequently moving toward change at an appropriate time (Dart, 2010). Motivational interviewing has been shown to be effective in increasing medication adherence in cardiac patients (Ogedegbe et al., 2008). Also, text messages have been effective in improving the use of prescribed cardiac medications among 65% of patients at six months (Wald, Bestwick, Raiman, Brendell, & Wald, 2014). Understanding the reasons for poor adherence may suggest approaches to novel interventions.

### **Theoretical framework guiding the study**

This study will use Bandura's social cognitive theory to enhance the refinement of self-efficacy (Bandura, 1977) and to examine the effects of individual, behavioural and environmental factors on medication adherence. According to the theory, self-efficacy is the pivotal determinant in influencing a person's particular behaviour, directly affecting one's actions and impacting on other determinants (Bandura, 1977, 2004). Bandura (2004) notes that self-efficacy determines the expected outcomes of people's behaviours. Reciprocal determinism is the basic organising principle of behaviour change proposed by this social cognitive theory, with continuous, functional interaction between the environment, the individual and behaviour (Bandura, 1998) (Figure 1). It assumes that a change in knowledge of health risk and benefits is essential, but requires additional impacts for change to occur (Munro, Lewin, Swart, & Volmink, 2007). Other determinants of behaviour change include behaviours, outcome expectations, expected benefits, beliefs and goals, and perceived facilitators and barriers. The theory proposes that if people perceive that they have outcome control, appropriate behaviour will follow, with sufficiently high self-confidence to overcome otherwise insurmountable barriers (Armitage & Conner, 2000).

Using a theoretical basis to explain relationships between study variables is important when designing effective behavioural change studies (Short, James, & Plotnikoff, 2013). Appropriately designed interventions that employ multiple strategies, such as motivational interviewing to encourage behaviour changes and text messaging strategies to reinforce behaviours, are likely to achieve

significant increases in medication adherence in cardiac patients (Al-Ganmi, Perry, Gholizadeh, & Alotaibi, 2016).

## **Methods**

### **Aim and hypothesis**

The study aims to use a pilot randomised controlled trial (RCT) to test the hypothesis that a theory based, nurse-led, multi-faceted intervention comprising motivational interviewing techniques and text message reminders in addition to standard care will better promote medication adherence in cardiac patients compared to standard care alone. Underpinning evidence and assumptions of the hypothesis are that:

- 1) A high proportion of patients fail to adhere to their cardiovascular medication regimens.
  - 2) Medication adherence self-efficacy, patient beliefs, and lack of social support are predictive factors associated with non- adherence to medication.
  - 3) High quality evidence supports the use of multi-faceted interventions comprising of motivational interviewing counselling combined with text messaging reminders to promote medication adherence.
- The pilot study will assess self-reported adherence or non-adherence to cardiovascular medication in patients referred to a cardiac rehabilitation program following hospital admission for an acute cardiac event and test the feasibility of the intervention. Medication non-adherence has been defined as ‘taking less than 80% of prescribed doses and can also include taking too many doses’ and it is associated with an increased risk of poor health, adverse clinical events and death (Nieuwlaat et al., 2014). The study will examine the role of individual, behavioural and environmental factors in predicting medication non-adherence in patients with CVD.

### **Study design**

This is a mixed methods study which includes a nested, pilot RCT. Both qualitative and quantitative methods are required to address the study’s aims and hypothesis. The use of mixed methods is valuable to provide a fuller picture of the topic and to transcend the limitations of each of the methods used singly (Borkan, 2004; Creswell, Fetters, & Ivankova, 2004).



In this study, data collection will occur sequentially: quantitative data collection followed by qualitative data collection will occur for the exploratory phases that will provide the explanatory power in support of the final (RCT) intervention testing phase: (QUAN + qual) → QUAN. Results from the exploratory phases (survey design and semi-structured interviews) will inform the fine tuning of the intervention in the third phase.

This multi-method study will entail three interrelated phases:

**Phase one:** The survey is designed to identify cardiac patients' patterns of medication adherence and their associated degree of adherence. The purpose of the survey is to gather quantitative data about medication adherence, patient behaviours, beliefs and other associated factors, including demographic data which will inform intervention and form baseline data.

**Phase two:** A descriptive qualitative study will explore the phenomena of cardiac patients' adherence to medications and how they respond to factors that affect medication adherence. Using semi-structured interviews, patients' views of their cardiac medications will be explored as well as the factors that influence their medication adherence.

A semi-structured interview format was chosen because of its flexibility in collecting self-reporting data (Cohen & Crabtree, 2006), enabling participants to talk freely about issues related to their medication adherence and telling stories in their own words. Semi-structured in-depth interviews will involve open-ended questions to elicit detailed narratives and stories (Whiting, 2008). This will provide in-depth understanding to supplement and explain quantitative results from Phase one.

Details of Phase one and Phase two data will be used to inform motivational interviewing techniques and to tailor the interventions to individual patients' needs to better support their adherence to cardiac medications.

**Phase three, a pilot RCT:** Participants identified as non-adherent to their medications in Phase one (based on Medication Adherence Questionnaire [MAQ] scores) and Phase two data (themes and patterns of medication adherence/non-adherence) will be invited to take part in this pilot trial. This will pilot test the feasibility and effectiveness of a multi-faceted intervention strategy, including motivational interviews plus text message reminders, to influence adherence to their cardiac medication regimes. The RCT will test and compare differences in outcomes between the standard care delivered

by a cardiac rehabilitation program and the same program augmented by this multi-faceted intervention. The feasibility of conducting a multi-faceted behavioural intervention in a busy cardiac rehabilitation setting will be investigated. We also sought data to determine the effect size for sample-size calculation as we could only extrapolate an estimated effect size from a somewhat similar trial for the sample size calculation of this pilot study. Data are currently lacking for full-scale trial of this approach among cardiac rehabilitation patients.

### **Study setting and participants**

The study will be carried out in the cardiac rehabilitation centre of a tertiary referral hospital in Sydney, Australia. Participants will be cardiac patients referred to a cardiac rehabilitation program following their admission for an acute cardiac event; those participating in the pilot trial will be randomly allocated to receive either the intervention plus standard care or standard care only. Inclusion criteria are: 18 years of age or older; diagnosed with cardiac disease and referred to the hospital cardiac rehabilitation program; currently taking at least one cardio-protective medication, and having primary responsibility for taking their own medications (i.e. not reliant on a carer). Participants must be able to read, speak and understand English, have a personal mobile phone, and be able to receive and reply to phone calls and text messages. Patients who are blind, deaf or unable to consent to receiving text messages will be excluded. Those clinically judged to have cognitive impairment that limits their ability to understand and answer the study questions will also be excluded.

### **Sample size determination**

The sample size for the pilot RCT was based on data from Ma, Zhou, Zhou, and Huang (2014). Using a two-sided test, moderate effect size with  $\alpha = 0.05$ , and power = 0.80, nine participants are required in each group. Allowing for 50% loss, a total of 28 cardiac patients will be needed for the pilot RCT.

Around 350 patients per year (30 per month) are estimated to attend the cardiac rehabilitation centre. Pilot data indicate around one third are considered non-adherent to medications. If 50% of eligible patients agree to participate, recruitment will progress at five participants per month (a rate of recruitment easily manageable for the researcher): it will take six months to enrol 28 participants, so

the study will take approximately six months for recruitment and six more months for intervention and follow-up.

### **Study procedures and data collection**

Data collection will take place at baseline and at six months, and changes in medication adherence will be compared within and between groups to determine any intervention effect. The Consolidated Standard of Reporting Trials (CONSORT) diagram of study processes is presented in Figure 2. Baseline survey and interview data will be collected during patients' hospital attendance for a cardiac rehabilitation session. Pilot RCT participants will repeat the Phase one survey via telephone interview at six months post-randomisation to collect the follow-up data; three additional open-ended questions (see Appendix 1) will explore participants' experiences of the motivational interview and the text messaging, and enquire whether anything else might have helped adherence.

In Phase two each interview will involve a face-to-face meeting for an interview guided by a set of questions or topics (Polit & Beck, 2004). Interviews will be arranged with participants using preferred communication methods with reminders two days beforehand. The guide for the individual semi-structured interviews can be found in Appendix 2. Data collection, transcription and analysis will be conducted, with questions modified in light of responses and emergent themes (Braun & Clarke, 2006).

### **Recruitment, enrolment and consent**

Recruitment will occur under the supervision of the clinical nurse consultant for cardiac rehabilitation, with the agreement of the director of nursing and the cardiology consultant. Patients referred to the cardiac rehabilitation program will be screened using the study inclusion/ exclusion criteria by the clinical nurse consultant at their first session. Eligible members of a consecutive cohort of patients who express interest in the project will be referred to the researcher, who will explain the study phases and provide an information statement and consent form. Completion of the survey will identify patients who are non-adherent with at least one cardiac medication, based on their answers to the MAQ with their non-adherence confirmed and detailed at Phase two by semi-structured interview. At the conclusion of

the semi-structured interview (Phase two), eligible participants will be informed about Phase three, the pilot RCT, and invited to participate.

The researcher will obtain written informed consent from participants for Phases one and two; similar consent to participate in the pilot trial will be obtained separately. Participants will receive a folder at enrolment, including written information about the study and a copy of their consent form, to supplement the face-to-face explanation of the study.

### **Randomisation and blinding processes**

In the pilot RCT, participants will be randomly assigned to either intervention or control group after they have consented to the trial phase. A computerised random number generator will be used to generate the random sequence. Using permuted blocks equal numbers of participants will be assigned to each group. Sequentially numbered sealed envelopes will be used to conceal the sequence until participants are assigned. Neither the participants nor the researcher can be blinded to the group allocation because of the nature of the behavioural intervention. A behavioural intervention such as motivational interviewing is not easily delivered blinded, and it is unlikely that cardiac patients in a cardiac rehabilitation program would not know which intervention they are receiving (Page & Persch, 2013). Outcome data are self-reported, but the assessor who will collect the outcome data will be blinded to study allocation to reduce potential bias.

### **The study intervention**

Approaches such as motivational interviewing aim to encourage behaviour change through influencing individual's feelings, thoughts, and confidence to change their behaviours, for example: adhere to a recommended medical regimen. The technique facilitates behaviour change by resolving patients' ambivalence to change (Miller & Rollnick, 2002). Motivational interviewing has been incorporated into several successful medication adherence interventions (Solomon et al., 2009). Using this technique, a wide variety of medication non-adherence factors are targeted, enabling patients to reflect on perceived barriers and search for solutions (Easthall, Song, & Bhattacharya, 2013). The interviewing 'elicits a range of possible actions and affirms the patient's autonomy to make informed choices' (Riegel et al., 2016, p. 3). Self-efficacy, one of the targeted factors, predicts adherence to medications, and this may

be mediated by patients' beliefs about their ability to cope, to locate optimistic changes in their social relations and to improve their individual confidence (Luszczynska, Sarkar, & Knoll, 2007). Social cognitive theory has previously been applied to examine medication adherence among CVD patients (Haskell et al., 1994), to foster individuals' medication adherence by setting goals and creating firm commitments to them, thereby encouraging patients to exercise more control over behaviours. In turn patients can come to believe they have a higher ability to adhere to their medications (Smith, Rublein, Marcus, Brock, & Chesney, 2003).

Text messaging has been widely used to improve health behaviours across multiple diseases (Spoelstra et al., 2015). It has been used to improve medication adherence by affecting different elements of cognition and evoking attention and an automatic response (Yiend, 2010). Text Messaging is widely available low-cost, patient friendly, requires low technological expertise and is applicable in a diverse range of health behaviours, acting as a safety-net for medication reminders (Cole-Lewis & Kershaw, 2010; Zallman, Bearse, West, Bor, & McCormick, 2016).

### **Intervention arm**

Participants in the intervention group will receive current standard care through the cardiac rehabilitation program plus behavioural counselling about medication adherence using motivational interviewing and text reminders. The current cardiac rehabilitation program includes a single one-hour information session on cardiac medication. The content received by both group participants will be recorded and compared to check for equivalence between the groups.

Each patient in the intervention group will receive approximately 30 to 40 minutes of a single motivational interview-style counselling session (Ma et al., 2014). The essence of motivational interviewing is for the counsellor to be simultaneously sympathetic and supportive, as well as directive in moving patients toward behaviour change by strengthening their reasons to change (Levensky, Forcehimes, O'Donohue, & Beitz, 2007). As part of the counselling, the researcher will provide information that the patient may need, and explore barriers that keep the patient from adhering to the medication regimen (Dart, 2010). A structured counselling script will be designed that can be tailored to medication adherence characteristics of individual patients (Dart, 2010). Examples of the content of

the session are available in Appendix 3. The sessions will be audiotaped and reviewed by a clinician qualified in motivational interviewing to ensure fidelity (Ma et al., 2014).

Text message reminders will be sent daily for the first two weeks, then on alternate days for fortnight, then once a week for the next five months, for a total of six months (Wald et al., 2014). The content will vary according to each patient's non-adherence factors. Examples are supplied in Table 1.

### **Control arm**

For the period of the study, patients in the control arm will be provided only with current standard care, which includes the provision of cardiac care knowledge and recommendations to enhance medication adherence and to promote healthy lifestyles; they will complete the same surveys as the intervention arm at baseline and at six months.

### **Outcomes**

The primary outcome is medication adherence/ non-adherence at six months. Medication adherence will be determined based on participants' responses to the MAQ (Morisky, Green, & Levine, 1986). Patients with a sum score of 1-2 will be considered 'adherent'; those with a score of 3 - 4 as 'non-adherent' (Morisky et al., 1986).

Secondary outcomes include identification of those factors exerting a significant influence on medication adherence, such as behaviour (self-regulation), beliefs (general harm; general overuse; specific necessity; and specific concerns), social support and self-efficacy using a combination of instruments, outlined below.

To assess the acceptability of the intervention at six months, the researcher will telephone each member of the intervention group to evaluate their experience of the interview and text messages (see Appendix 1).

### **Study instruments**

The survey will include a set of questionnaires designed to gather data about medication adherence and patient behaviours, beliefs and other factors associated with adherence/ non-adherence. The survey will be paper based, self-administered, and suitable for participants with low literacy skills.

Sociodemographic and health data will be collected: age, gender, living arrangement, level of education, ethnicity; co-morbidities.

The use of different instruments in this study will enable comprehensive study of factors contributing to medication non-adherence in patients with CVD, including behavioural and psychological factors. Motivational interviews in the RCT phase will focus on the identified non-adherence factors for each individual patient.

Medication non-adherence will be assessed by the Medication Adherence Questionnaire (MAQ) (Morisky et al., 1986), which is designed to measure medication adherence behaviour and barriers such as forgetfulness, carelessness, adverse effects and efficacy. It includes four simple dichotomous questions, assigning one point for each yes response; total scores are categorised as: 0= high; 1-2= medium, and 3-4= low medication adherence behaviours (Morisky et al., 1986).

The Adherence to Refills and Medications Scale (ARMS) (Kripalani, Risser, Gatti, & Jacobson, 2009) will be used to determine medication adherence behaviour in terms of self-regulation. The ARMS is a 12-item scale: an eight-item medication-taking subscale assessing correct self-administration for the prescribed medications; and a four-item prescription refill subscale evaluating the patient's ability to replenish medications on schedule. Each item is scored on a four-point scale ranging from 1= none of the time to 4= all the time on a four-point Likert scale, with higher numbers demonstrating better refill ability for medications on schedule (Kripalani et al., 2009).

The Belief about Medicine Questionnaire (BaMQ) (Horne, Weinman, & Hankins, 1999) elicits information on patients' beliefs about medications which may be adherence-related. It identifies whether the patient believes in the necessity of their medicines or has concerns about them. The study will use the short (eight-item) version of the BaMQ developed by Horne et al. (1999), composed of four subscales of two items each, assessing: specific necessity, specific concerns, general overuse and general harm. Answers range from 1= strongly disagree to 5= strongly agree on a five-point Likert scale; scores are summed to derive a total score, with higher scores indicating more positive beliefs.

The Medication Adherence Self-Efficacy Scale-Revised (MASESE-R) (Fernandez, Chaplin, Schoenthaler, & Ogedegbe, 2008) consists of 13 items that evaluate an individual's ability to adhere to medications under various challenging circumstances. Twelve items examine patients' confidence in

taking medications in specific circumstances (e.g. with family, in public places, feeling well), and one assess the ability to take medications as part of the everyday routine. Each item is scored on a four-point Likert scale, ranging from 0= not at all sure to 3= extremely sure. A single score is derived from the mean of all items, with greater self-efficacy indicated by high scores (Fernandez et al., 2008).

The Medication Specific Social Support (MSSS) scale (Lehavot et al., 2011) is an eight-item survey of medication-specific social support to identify how often others help patients with their medication, scored for each item ranging from 0= never to 4= very often. A single mean score is presented as a medication-specific index of support (Lehavot et al., 2011).

### **Validity and reliability**

The MAQ is a validated four-item tool suitable for a wide range of conditions involving cardiac diseases (Nguyen, Caze, & Cottrell, 2014). Its validity and reliability has been determined in patients with hypertension, with a reported acceptable internal consistency of  $\alpha = 0.61$ , sensitivity 0.81 and specificity 0.44 (Lavsa, Holzworth, & Ansani, 2011); it has also been validated in patients with heart failure, CVD and dyslipidemia (Afonso, Nassif, Aranha, DeLor, & Cardozo, 2006). MAQ score was found to be a significant independent predictor of cardiovascular nonadherence in a multivariate logistic regression model (Shalansky, Levy, & Ignaszewski, 2004) (Table 2).

The ARMS subscales are highly correlated with the Morisky medication adherence four-item scale, and with medication refill adherence (Kripalani et al., 2009). The ARMS has been validated in patients with cardiovascular disease and other chronic diseases (Kripalani, Henderson, Jacobson, & Vaccarino, 2008). Among patients with low literacy skills (Kripalani et al., 2009) it has demonstrated high internal consistency using Cronbach's  $\alpha$  and test-retest reliability, set out in Table 2 (Kripalani et al., 2009).

The BaMQ has been shown to correlate significantly with other adherence-related questionnaires such as MAQ, the Morisky medication adherence scale, and the medication adherence rating scale (MARS-5) (Gatti, Jacobson, Gazmararian, Schmotzer, & Kripalani, 2009; Horne et al., 1999; Mårdby, Åkerlind, & Jörgensen, 2007). Each BMQ subscale has been evaluated for internal consistency using Cronbach's  $\alpha$  (Horne et al., 1999). Demonstrating criterion-related validity, the four



BaMQ categories correlated highly with patients' beliefs about the adverse effects of medication and specific concerns as assessed by the Sensitive-Soma Scale administered to general medical and cardiac groups (Table 2) (Horne et al., 1999).

The MASES-R has been found to correlate significantly with electronic medication adherence records (MEMS) at three-months, confirming its predictive validity (Fernandez et al., 2008). The concurrent validity of the MASES-R has also been confirmed (Table 2).

## **Data Analysis**

**Phase one:** Descriptive statistics will be used to analyse data related to the patients' baseline characteristics. Data will be checked and cleaned prior to entry into SPSS for Windows version 23. Measures of central tendency and dispersion will describe the values of medication adherence, medication adherence self-efficacy, and beliefs about medication. Bivariate analyses will be conducted to examine factors potentially associated with medication non-adherence. Factors and behaviours related to medication non-adherence will be examined by logistic regression. Two sided tests will be conducted with significance set at .05.

**Phase two:** Qualitative data will be analysed inductively using thematic analysis (Sim, 1998). This approach will focus on recognising, analysing and reporting recurrent patterns (themes) and subcategories within the data (Liamputtong, 2013). Simultaneous collection, transcription and analysis allows the researcher to build on emerging themes (Polit & Beck, 2014). Data will be examined and compared to identify similarities and differences by reading and searching within transcripts and across the data set (Polit & Beck, 2014). QSR NVivo software will be used to code and construct thematic analysis (Braun & Clarke, 2006). A similar but separate process will be employed with the data collected in response to the open questions at six months.

**Pilot RCT phase:** Data will be analysed according to the intention to treat principles. Using survey and demographic data, the two groups will be compared at baseline and any differences taken into account during the outcome assessment. Paired samples t-test analysis will be used to test within-group differences on the medication adherence questionnaire scores (MSSS, MAQ, ARMS, BaMQ, and MASES-R), and independent sample t-test will compare the scores of the intervention and control

groups. Multinomial regression analysis will be applied to identify variables that significantly influence adherence to medication, such as self-efficacy, beliefs, level of confidence, or social support. Variables exerting significant influence on medication adherence in bivariate analysis will be entered in the regression analysis, with significance set at  $P < 0.25$  for the preliminary bivariate analysis and  $P < 0.05$  for the regression analysis (Polit., 1996).

### **Ethical considerations**

Approvals to conduct this study were granted by the appropriate health district and university Human Research Ethics Committees in June 2016 (reference numbers: 16/085 (HREC/16/POWH/218; ETH16-0635). The study is registered as a clinical trial (ACTRN12616000910404) on [www.anzctr.org.au](http://www.anzctr.org.au).

### **Discussion**

Patients with CVD often have multiple chronic illnesses requiring multiple prescriptions. Studies of long-term medication adherence outcomes are limited (Bansilal et al., 2016) although non-adherence is common in these patients and accounts for substantial morbidity and mortality (Albert, 2008). Adequate medication adherence may help improve quality of life by improving disease outcomes (Luszczynska et al., 2007). Better medication adherence may be achieved with interventions that address the known multiple factors of non-adherence, including lack of patient knowledge of perceived benefits, the perceived harm of medications, poor medication management and inadequate social support (Calvert et al., 2012).

Medication adherence interventions for patients with CVD have been shown to be effective when delivered by nurses, who should play an active role in designing and applying such interventions (Albert, 2008; Chase et al., 2016). A recent systematic review emphasised that cardiac rehabilitation and prevention programs should encompass a dedicated strategy for medication adherence; at present, the majority of these programs do not measure and report adherence outcomes appropriately (Santo et al., 2016). There is scope for medication adherence interventions using techniques focused on promoting behavioural change to become part of routine health care (Easthall et al., 2013). This study aims to evaluate the effectiveness of theory-based, nurse-led, multi-faceted interventions for medication

adherence in a robust pilot trial using a RCT design, in line with the findings and recommendations of the recent review of medication adherence interventions for this population by Al-Ganmi et al. (2016).

### **Limitations**

This study has some potential limitations. Firstly, use of a multi-faceted intervention, while recommended as likely to increase the success of intervention as a whole, challenges researchers to identify the contribution of the individual components. This study attempts to address this by seeking participants' experiences of each separate component of the intervention. Secondly, measuring medication adherence through self-reporting may introduce a response bias presenting potential problems with reliability. Also, social desirability bias is possible due to lack of blinding. Self-reporting is a commonly used method of outcome assessment for medication adherence as it is acceptable to participants and imposes a minimal burden. It also has the potential to explore medication adherence behaviour, adherence-related barriers and beliefs about medicines which may support beneficial medication adherence assessment in chronic disease management. Finally, participants are predominantly older adults who will be asked to spend 20 - 30 minutes answering 45 questions in Phase one (repeated at six months for participants in the intervention group) and 30-45 minutes in the Phase two interview. This may challenge their stamina, patience and tolerance.

### **Conclusion**

Medication non-adherence among patients with CVD is a major problem. Multi-faceted medication adherence interventions comprising motivational interviews and text reminders may improve adherence to cardiac medication regimens by targeting individual behaviour change. This pilot study will provide important information about techniques appropriate for use by nurses to support medication compliance in their patients. Findings may support development of further trials of this intervention in out-patient cardiac care settings ahead of translation into routine clinical care. It may also be suitable for implementing in other health care areas and long-term patient groups.

If this and further trials are successful, important next steps will be to consider the potential for widespread roll-out, including training nurses in motivational interviewing techniques. Software compatible with organisations' routine data programs will be required for automatic delivery of text

messages. The time requirement of the intervention will need to be considered for staffing rosters and patient appointments. A full cost-effectiveness analysis is therefore recommended.

This protocol sets out the essential first steps for what may be an exciting new development in the contribution of nursing staff to delivering a substantial benefit to a sizeable patient group where there is clear potential for significant improvement in adherence.

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