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Improving adherence using combination therapy (IMPACT): Design and protocol of a randomised controlled trial in primary care

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ABSTRACT

Background: Cardiovascular disease (CVD) is the leading cause of death, and principal reason for the large difference in life expectancy between indigenous Māori and the non-indigenous population in New Zealand. CVD guidelines recommend that people who are at high risk or who have had previous CVD should be offered aspirin, blood pressure lowering and lipid lowering therapies. However, prescribing and adherence rates are low and CVD events remain high.
Aim: To assess whether a medication strategy using a fixed dose combination pill ('polypill') could improve prescribing and adherence to recommended medications, lower blood pressure and improve lipids compared with current care over 12 months.
Methods: IMProving Adherence using Combination Therapy (IMPACT) is an open-label randomised controlled trial comparing a once-daily polypill containing four preventive medications with usual care. Six hundred participants who have had previous CVD events or are at high risk of CVD will be enrolled, including 300 Māori. Participants are identified, enrolled and prescribed either the polypill or current medications at their usual primary health care practice, with medications (including the polypill) dispensed through local community pharmacies. The polypill contains 75 mg aspirin, 40 mg simvastatin, 10 mg lisinopril and either 12.5 mg hydrochlorothiazide or 50 mg atenolol. Primary outcomes are adherence to guidelines-recommended medications and changes in systolic blood pressure and low density lipoprotein at 12 months. Secondary outcomes include other lipids, medication dispensing, barriers to adherence, CVD and other serious adverse events, quality of life and prescriber acceptability. The trial is registered with the Australian New Zealand Clinical Trial Registry (ACTRN12606000067572).

1. Introduction

Globally, cardiovascular disease (CVD) is the leading cause of death, and a major and increasingly important contributor to the overall burden of disease [1]. In New Zealand, CVD is also the principal reason for the large difference in life expectancy between indigenous Māori and the non-indigenous population [2–4]. CVD guidelines recommend that people who are at high risk or who have had previous CVD should be offered

Abbreviations: CVD, Cardiovascular Disease;IMPACT, IMProving Adherence using Combination Therapy;LDLc, Low Density Lipoprotein cholesterol; RHP, Red Heart Pill;SAE, Serious Adverse Event;WHO, World Health Organisation.

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antiplatelet, blood pressure lowering and lipid lowering therapies, which can substantially reduce risk of future CVD [5–8]. However, many high risk patients who could benefit from these medications are not receiving them. For example, a recent New Zealand study found that only 67% of those with previous CVD attending CVD risk assessment at their primary care physician were prescribed both blood pressure lowering and lipid lowering medications [9]. Only 60% of New Zealand patients were taking a statin regularly in the 12 months following an acute coronary event in a national sample [10]. A nationally representative survey in Australian primary care found that only 50% of those with previous CVD were prescribed all three categories of preventive medications [11]. Similar low rates have been found in Europe and North America [12–14]. Amongst patients without previous CVD but at high risk, prescription rates are even lower [11,13,15].

Even if prescribed, long-term adherence to medications is low, further compromising the preventive potential of these medications [16–19]. A 2003 World Health Organisation (WHO) report estimated that less than 50% of those prescribed long-term medications for chronic conditions take their medication regularly [20]. Four key potentially modifiable barriers identified in a recent systematic review of barriers to medication adherence are: cost, regimen complexity, medication beliefs and, amongst patients with diabetes, depression [21]. The WHO report recommends that interventions to improve adherence should be developed and could significantly improve health outcomes.

A fixed dose combination pill, or 'polypill', that combines four preventive medications for high risk individuals is one such strategy, as it simplifies the medication regimen both for prescribers and patients and could reduce cost for health funders and patients [22]. Preliminary placebo-controlled trials of the polypill in moderate risk individuals have demonstrated that this strategy appears to be feasible and well tolerated by such patients [23,24]. Randomised controlled trial evidence is required in high risk individuals, for whom the combination of aspirin, blood pressure lowering and lipid lowering therapies are indicated, to assess the efficacy and safety of a polypill-based approach in this group. Understanding the role of such a strategy in reducing inequalities in the burden of CVD for indigenous and other high risk groups is also important.

IMProving Adherence using Combination Therapy (IMPACT) is a randomised controlled trial designed to assess whether a polypill-based strategy improves adherence and CVD risk factors (blood pressure and lipid profile) compared with usual care amongst Māori and non-Māori patients at high risk of CVD in a New Zealand primary care setting. IMPACT's protocol has been used as the basis for "sister" trials, using the same polypill, in Australia [25], Europe (United Kingdom, Ireland and the Netherlands) and India, to assess consistency of effect across different contexts and populations.

2. Methods

IMPACT is an open-label, randomised, controlled trial of 600 participants (including 300 Māori) at high risk of CVD. Participants are randomised to polypill-based care or usual care and followed until 12 months after the last participant has been randomised. Recruitment commenced mid 2010 and will be completed by early 2012. The duration of follow-up will therefore range from 12 to 30 months, with an estimated mean of 18 months, finishing early 2013 (Fig. 1).

2.1. Identifying and recruiting participants

Primary health care practices in Auckland and Waikato regions of New Zealand with high enrolment of Māori are targeted for this trial. The electronic medical records of practices that agree to participate are systematically searched for potentially eligible patients. Patients are invited onto the trial from the practice by mail and subsequently contacted by a research nurse. Given that Māori comprise 15% of New Zealand's population, a weighted sampling frame is used when screening for and identifying high-risk patients within practice electronic medical records.

2.2. Trial population

Enrolled and consenting patients are eligible for inclusion if all of the following criteria are satisfied: aged 18–79 years;

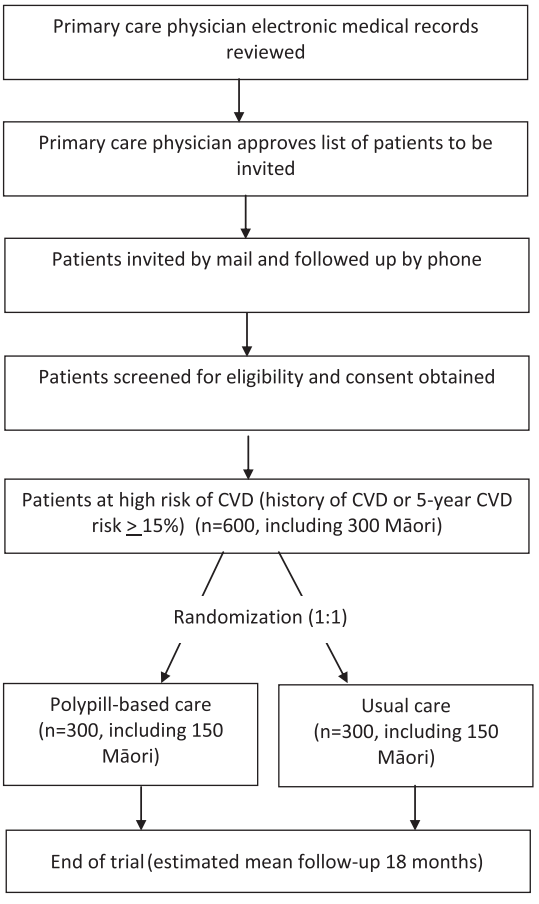

Fig. 1. Trial design schematic. *Primary outcomes:* Adherence (self-reported current use of antiplatelet, statin and combination [≥2] blood pressure lowering therapy) and change in systolic blood pressure and fasting LDLc, at 12 months. *Secondary outcomes:* Dispensing of statin and combination blood pressure lowering agents, self-reported barriers to adherence, serious adverse events, CVD events, reasons for stopping CVD medications, quality of life (EuroQol 5D), prescriber acceptability, change in other serum lipid fractions and healthcare resource consumption.