



## Predictors of health care use among patients with or at high risk of atherothrombotic disease: Two-year follow-up data



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### ABSTRACT

**Background:** Atherothrombotic diseases are the leading health problems in the world, both in terms of morbidity and mortality. This study aimed to identify and quantify the predictors of medication, hospital and outpatient service use among patients with or at high risk of atherothrombotic disease.

**Methods:** Two-year follow-up data were analyzed for 2873 Australian participants of the Reduction of Atherothrombosis for Continued Health (REACH) registry. The analysis was performed using generalized linear models with Poisson and Gamma distributions and log link function.

**Results:** Participants with hypercholesterolemia, diabetes, hypertension, atrial fibrillation (AF), and history of coronary artery disease (CAD) used more medications ( $p < 0.0001$ ). The presence of diabetes predicted higher number of outpatient visits (RR = 1.09, 95% CI: 1.07–1.11), as did AF (RR = 1.10, 95% CI: 1.08–1.12). The presence of peripheral artery disease (PAD) regardless of ankle brachial index (ABI) status (abnormal or normal) increased the use of outpatient visits (RR = 1.24, 95% CI: 1.20–1.29 and RR = 1.12, 95% CI: 1.08–1.15), compared to those without PAD. Similarly, the presence of PAD regardless of ABI status increased the risk of vascular interventions, including coronary angioplasty, carotid surgery, amputation affecting lower-limb and peripheral bypass graft (RR = 3.64, 95% CI: 2.01–6.60) (RR = 2.8, 95% CI: 1.6–4.92) compared to patients without PAD.

**Conclusions:** The presence of PAD regardless of ABI status predicts a higher number of outpatient visits, non-fatal cardiovascular endpoints and vascular-interventions, while diabetes predicts higher pharmaceutical use and outpatient visits. AF predicts the higher number of outpatient visits and non-fatal cardiovascular events.

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### 1. Introduction

Chronic conditions such as atherothrombotic disease remain one of the most significant health problems in terms of morbidity and mortality in the world, and also impose a large burden on health care budgets [1–3]. Despite improvements in quality of life due to interventions, patients with atherothrombotic disease continue to be undertreated and do not receive secondary preventive medications as per recommended guidelines [2,4]. Furthermore, the prevalence of disease and excess costs of care are expected to increase even further due to rapidly ageing population and high prevalence of abdominal obesity which in turn will pose a substantial burden [5] among this group of population.

While previous studies have estimated the cost burden of elderly patients with atherothrombotic disease in acute care settings, few studies have identified and quantified independent major predictors of health care use among elderly patients with or at high risk of atherothrombotic disease treated in community settings [4,6–11]. Data on such predictors would inform the cost-effectiveness of decision modelling, and hence help prioritization of healthcare services within limited budget planning.

Contemporary data from Australian patients enrolled in the Reduction of Atherothrombosis for Continued Health (REACH) registry have indicated that hypertension, hypercholesterolemia, diabetes, obesity and established cardiovascular disease were independent drivers of increased pharmaceutical use and related costs at baseline [4]. However, the long-term predictors of outpatient visits and hospitalizations have not been identified and quantified previously in community settings. Therefore, the aim of the current study was to identify and quantify independent predictors of health care use (pharmaceutical, outpatient

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visits and hospitalization) using two-year follow-up data from the Australian REACH registry.

## 2. Materials and methods

### 2.1. The REACH registry

The international REACH registry has been described previously in details [12,13]. A total of 2873 participants were enrolled from Australia, drawn from general practices across the country [11,14]. Every participating general practice recruited a maximum of 15 participants over a period of four months from March to June 2004. Participants were seen by a study nurse who performed initial screening and reviewed and entered their medical records.

### 2.2. Study population

Patients were eligible for inclusion in the study if they were aged  $\geq 45$  years, and had the presence of coronary, cerebrovascular or peripheral arterial disease or  $\geq 3$  documented cardiovascular risk factors for atherothrombosis. Risk factors for atherothrombosis comprised diabetes, diabetic nephropathy, ankle-brachial index  $\leq 0.9$ , asymptomatic carotid stenosis  $\geq 70\%$ , and carotid intima media thickness of two times or more adjacent sites, systolic blood pressure  $\geq 150$  mm Hg (despite treatment), hypercholesterolemia managed with medication, current smoking of  $\geq 15$  cigarettes per day, and age  $\geq 65$  years for men or  $\geq 70$  years for women [12].

The criteria for coronary artery disease (CAD) were: current angina with documented CAD; history of unstable angina with documented CAD; previous coronary angioplasty/stenting; previous coronary artery bypass graft; and previous myocardial infarction. The criteria for cerebrovascular disease (CerVD) were: documented diagnosis of ischemic stroke or transient ischemic attack (reported by either the neurologist or the hospital). The criteria for peripheral artery disease (PAD) were: current intermittent claudication with ankle-brachial index of less than 0.9 and/or a history of intermittent claudication together with a previous intervention, such as angioplasty, stenting, atherectomy, peripheral arterial bypass grafting, or other vascular interventions, including amputations [12,13]. If participants were involved in clinical trials or hospitalized during the study period they were excluded from the REACH registry.

### 2.3. Data collection and evaluation

Baseline data were collected from an internationally standardized case report and included information on: demographics, formal education, employment status, previous medical history, risk factors and medications prescribed for cardiovascular disease; physical examinations were also undertaken and blood sampled for biochemical markers was collected. Follow-up clinical events, hospitalization, outpatient visits and cardiovascular medication were re-evaluated at 12 and 24 months.

### 2.4. Medication use

Study nurses recorded medication use through a review of practice notes and via telephone interviews. Detailed information on use of prescribed medications in the Australian REACH Registry has been reported elsewhere [4,15].

### 2.5. Out-of-hospital healthcare encounters

Out-of-hospital healthcare encounters included visits to general practitioners, rehabilitation clinics, ancillary services (such as physiotherapy), as well as blood tests and imaging (carotid Doppler, renal ultrasound, chest X-ray, computed tomography, angiogram and magnetic resonance imaging).

### 2.6. Clinical outcomes and hospitalization

Major non-fatal cardiovascular events were reported by participating clinician–investigators. Hospital admission records for all major cardiovascular events were confirmed and validated [12]. Non-fatal cardiovascular events comprised: non-fatal MI, non-fatal stroke, unstable angina, transient ischemic attack, other ischemic arterial event, congestive heart failure, or an episode of bleeding by 12 or 24 months of follow-up which led to hospitalization and transfusion. Vascular interventions which led to hospitalization were classified as: coronary artery bypass graft, coronary angioplasty/stenting, carotid surgery, carotid angioplasty/stenting, amputation affecting lower limbs, peripheral bypass graft, or any other intervention for PAD [12,13].

### 2.7. Ethics approval

The REACH registry was approved by the Royal Australian College of General Practitioner, and the Institutional Ethics Committee of Monash University. All enrolled participants gave their written informed consent to be involved in the study.

### 2.8. Statistical analyses

Statistical analyses were performed using STATA11 (StataCorp, TX, USA). Descriptive statistics were reported as  $N$  (%) for categorical variables (e.g. gender, education, etc),

mean (SD) for continuous, normally distributed data (e.g. age) and median with interquartile ranges (IQR) for ordinal or not normally distributed continuous data (e.g. number of medications, other healthcare services and number of hospitalization). The abnormal ankle brachial index (ABI) was defined as  $ABI < 0.9$ . Categories of patients with CAD, CerVD, and PAD were not mutually exclusive. Therefore, each clinical category was compared against all patients who were not in that category. All patients with follow-up data at one or two years were included in the analyses (2847 (99.68%) and 2734 (95.73%) respectively). The people who died during the first and second year were excluded from this analysis.

Multivariable regression analysis was used to determine factors associated with numbers of medication used, outpatient visits, non-fatal events and vascular interventions. The inclusion of the predictors was guided by either the results of bi-variate analysis or clinical importance based on evidence. Due to the nature of primary outcomes (number of services used), the analysis was performed using generalized linear models (GLM) with Poisson distribution and log link function.  $P$ -values of  $< 0.05$  were considered statistically significant for all tests.

Sensitivity analyses also were performed to identify the predictors of health care use in first and second year of follow-up.

## 3. Results

There were 2856 participants included in our sample. The majority of participants in the Australian REACH registry had established CAD (58.0%) at baseline. The average age of participants was 72.8 ( $\pm 8.9$ ) years. Polyvascular disease was present in 15.3% of participants. The prevalence of hypertension and hypercholesterolemia was high (Table 1). Patients with diabetes, obesity, and AF at baseline accounted for the 30.3%, 28.5%, and 13.2% of the cohort respectively.

Results of univariable analysis about individual predictors of medication use, outpatient visits, non-fatal events, and vascular intervention at two-year follow-up are presented in Table 2.

### 3.1. Predictors of medication use

Annual median number of medication use in Australian cohort was 4.2 with interquartile (IQR) ranges [2–5]. Number of individual medication used at 12 months of follow-up was shown in Appendix 1. Diabetes, hypercholesterolemia, hypertension, AF, and presence of CAD were predictors of medication use (in all cases,  $p < 0.001$ ) in the year one and two (Fig. 1). There were 17.0% ( $n = 66/2856$ ) of AF patients who did not have aspirin or other anticoagulants prescribed to them during the study period. Among those treated, 11.0% were on both medications and 71.0% were on either (aspirin or anticoagulants).

**Table 1**

Baseline demographics of patients in two years of follow-up analysis.

Variable	Total ( $N = 2856$ ), $N$ (%)
Age mean years (SD)	72.8 (8.9)
Male	1859 (65.0)
Unemployed/retired	2313 (81.1)
Education:	
1–12 years	1830 (64.1)
Trade/technical school	556 (19.5)
College/university	434 (15.2)
Diabetes	866 (30.3)
Hypertension	2217 (78.7)
Dyslipidemia	2216 (77.6)
Current smokers	195 (6.9)
Obesity (BMI $> 30$ )	826 (28.5)
History of CAD	2103 (73.6)
History of CerVD	667 (23.3)
History of PAD	257 (9.0)
Multiple risk factors	303 (10.6)
Atrial fibrillation	377 (13.2)

Note: results presented as percentage.

CAD—coronary artery disease, CerVD—cerebrovascular disease, PAD—peripheral arterial disease. Dyslipidemia—patients currently treated. Hypertension—patient with treated hypertension and history of hypertension. Diabetes—patient with type I and type II diabetes currently treated or a history of diabetes.

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