

A Retrospective Cohort Study On Prescribing Inequalities Of Evidence-based Pharmacotherapy Within Thirty Days After First Diagnosis Of Peripheral Arterial Disease In Scotland

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Abstract

Background

Prescribing of evidence-based pharmacotherapies (EBPs) for patients diagnosed with cardiovascular diseases (CVD) decrease mortality and disease progression, however prescribing inequalities remains an issue.

This study aims to describe the correlation between prescribing EBPs within thirty days after first diagnosis of peripheral arterial disease (PAD) and other factors such as age, sex, and socioeconomic status.

Methods

This study examined a linked database of primary and secondary care records in a sample population of 238064 people in Scotland. Patients with first time diagnosis of PAD were identified. Excluded patients who died within thirty days after first diagnosis.

To examine the association between prescribing EBPs and age, sex and socioeconomic, multivariable logistic regression was conducted.

Results

Through the study period 1997-2005, about 3385 (95.8%) patients were identified with first diagnosis of PAD had survived for 30 days. Increasing age associated with less opportunity of being prescribed EBPs, which persisted after adjustment to confounders. Patients older than 85 were less commonly prescribed EBPs. Prescribing EBPs were significantly less commonly among men compared to women (OR 0.73; 95% CI 0.59-0.91, $P < 0.004$), however negligible variation in prescribing EBPs between most deprived and least deprived.

Conclusion

Even though clinical trials and guidelines recommend the prescription of secondary treatment for every patient regardless of their gender or age, prescribing inequalities has existed.

Keywords: evidence-based pharmacotherapy and inequality, peripheral vascular disease secondary prevention, peripheral arterial disease.

الملخص

خلفية الموضوع

إن وصف العلاجات الدوائية القائمة على الأدلة (EBPs) للمرضى الذين تم تشخيص إصابتهم بأمراض القلب والأوعية الدموية (CVD) يقلل من معدل الوفيات وتطور المرض ، ولكن لا يزال وصف عدم المساواة يمثل مشكلة.

تهدف هذه الدراسة إلى وصف العلاقة بين وصف EBPs في غضون ثلاثين يومًا بعد التشخيص الأول لمرض الشرايين المحيطية (PAD) وعوامل أخرى مثل العمر والجنس والحالة الاجتماعية والاقتصادية.

أساليب

فحصت هذه الدراسة قاعدة بيانات مرتبطة بسجلات الرعاية الأولية والثانوية في عينة سكانية من 238064 شخصًا في اسكتلندا. تم تحديد المرضى الذين تم تشخيصهم لأول مرة باعتلال الشرايين المحيطية. يستثنى المرضى الذين ماتوا في غضون ثلاثين يومًا بعد التشخيص الأول.

لفحص العلاقة بين وصف EBPs والعمر والجنس والاقتصاد الاجتماعي ، تم إجراء الانحدار اللوجستي متعدد المتغيرات.

نتائج

خلال فترة الدراسة 1997-2005 ، تم التعرف على حوالي 3385 (95.8٪) مريضًا بالتشخيص الأول لاعتلال الشرايين المحيطية لمدة 30 يومًا. زيادة العمر المرتبطة بفرصة أقل لوصف EBPs ، والتي استمرت بعد التكيف مع الإرباك. كان المرضى الذين تزيد أعمارهم عن 85 عامًا أقل شيوعًا في وصف أدوية EBPs. كان وصف EBPs أقل شيوعًا بشكل ملحوظ بين الرجال مقارنة بالنساء (OR 0.73) ؛ 95٪ CI 0.59-0.91 ، $P < 0.004$ ، ومع ذلك فإن الاختلاف ضئيل في وصف EBPs بين الأكثر حرمانًا والأقل حرمانًا.

استنتاج

على الرغم من أن التجارب السريرية والمبادئ التوجيهية توصي بوصفة علاج ثانوي لكل مريض بغض النظر عن جنسه أو عمره ، إلا أن وصف عدم المساواة موجود.

الكلمات المفتاحية: العلاج الدوائي القائم على الأدلة وعدم المساواة ، الوقاية الثانوية من أمراض الأوعية الدموية الطرفية ، أمراض الشرايين الطرفية.

Introduction

Peripheral arterial disease (PAD) is a disease that may affect life quality and increase the risk of developing other cardiovascular disease (CVD). It is an atherosclerotic disease which increases in population older than 55 years old.¹⁻³

Pharmacotherapy treatment of PAD aims to reduce the risk of further CVD, improve quality of life and improve symptoms. For example, naftidrofuryl, pentoxifylline, and Cilostazol. A number of studies demonstrated that significant improvement in the maximal walk distance and pain-free associated with prescribing of cilostazol and naftidrofuryl.⁴⁻⁶ However, there was no significant effect on the walking distance between pentoxifylline compared to placebo.⁷

The risk of CVD and cerebrovascular disease increases in patients with PAD.⁸ Therefore, secondary prevention of evidence based pharmacotherapies (EBPs) including angiotensin-converting enzyme inhibitors (ACEI), antiplatelet and statins should be considered.^{9,10}

These EBPs associated with significant impact on lowering the risk of cardiovascular mortality, stroke, and myocardial infarction (MI) among patients with symptomatic PAD.^{9,11-14} Even though clinical trials demonstrated a positive effect of EBPs, various studies revealed that there are inequalities in prescribing these medications.

The study has the objective of describing the correlation between EBPs prescription within 30 days of the first diagnosis with peripheral arterial disease (PAD) and other factors such as age, sex, and socioeconomic status.

Methods

This research involved the use of a retrospective cohort study by examining a linked database of primary and secondary care records. Additionally, Scottish Morbidity Records (SMR) and Continues Morbidity Records (CMR) covering six percent of the Scottish population from 1997 to 2005.

Every diagnosis, primary or secondary health care clinic, was modified to show if the condition is a first-time diagnosis, persistent or recurrent. Every diagnosis was recorded using a Read code that was created as a medical term thesaurus.¹⁵ The Read codes entail five alphanumeric characters and start with a broad classification before narrowing to become more specific.¹⁵⁻¹⁷ Moreover, general practitioners also record prescribed medications in the CMR. Coding a new prescription can easily be inputted without assistance and as a result of the drugs prescribed may automatically be recorded as many generic trade names that are registered in the British National Formulary (BNF).^{17,18}

Secondary care data in Scotland is collected as a series of records at the individual level. The general type of healthcare in a hospital episode is denoted by the main record type. Data include patients' principal diagnosis and up to five comorbidities or secondary diagnoses, up to four operations, identifiable information, administrative details including hospital and consultant in charge, demographic information.

Identification of small area concentrations of multiple deprivations across Scotland is done by the use of an area-based measurement called the Scottish Index of Multiple Deprivation (SIMD).^{22,23}

The authority to carry out this study was granted by the Privacy Advisory Committee (PAC). The data set used included prescriptions, SMID scores, patients diagnosed in secondary and primary care, and deaths. The SIMD was classified from the least deprived quintile (1) to the most deprived quintile (10). The Read codes for primary care and the ICD9 and ICD10 for secondary care were used to identify first time diagnosis. Additionally, the British national formulary (BNF) codes were used in the identification of EBPs for the management of PAD. Patients who died within thirty days after first diagnosis were excluded.

Statistical analysis

To examine the independent effect of age, sex and socioeconomic status in prescribing EBPs within thirty days after first diagnosis, the multivariable logistic regression was conducted.

To avoid confounders influences the odds ratios were adjusted for year, socioeconomic, status sex, age group, comorbidities including diseases which may affect prescribing for PAD (COPD/asthma, renal failure, diabetes, hypertension, cancer, AF, HF, PAD, stroke, MI and angina), a drug prescribed prior to the first diagnosis and clustering of practices.

Results

Baseline demographic characteristics

Of 3532 patients were diagnosed with PAD, 2581 (73%) individuals with first PAD were identified in the primary care while 951(27%) individuals were identified in the secondary care. Of these, 3385 (95.8%) patients survived 30 days after the first diagnosis were eligible to be included in this study table 1.

Prescribing of evidence-based pharmacotherapy

A significant statistical difference in the odds of prescribing EBPs between the age groups for β -blockers (overall p-value = 0.01), statins (0.001) and aspirin (0.05). As can be seen in figure 1, compared to those younger than 55 years, elderly patients (≥ 85 years) were significantly less likely to be received ACEI/ARBs (odds ratio [OR] 0.36; 95%CI 0.17-0.78), and statins (OR 0.06; 95%CI 0.01-0.28).

As shown in figure 2, compared to women, men were significantly less commonly prescribed statins (OR 0.73; 95% CI 0.59-0.91, $p=0.004$). Moreover, men were less likely, but not significant, of being prescribed other medications, apart from β -blockers, peripheral vasodilators (PVDs) and calcium channel blockers (CCBs).

The variances in prescribing of EBPs according to the socioeconomic status are shown in figure 3. Patients living in more deprived areas were more likely received PVD prescription, compared to patients living in the least deprived areas. These patients, however, were significantly less commonly prescribed aspirin (OR 0.55, 95% CI 0.37-0.83).

Discussion

Few studies have investigated the prescribing of EBPs after a diagnosis of PAD. However, such studies have reported contradicting results in terms of the association between prescribing EBPs and socioeconomic status, sex, and age. This study was adjusted for various covariates and a prescription of the recommended pharmacological treatment. Prescription after first diagnosis was examined to ensure prescribed medication was given for a particular episode. This was done to avoid confusion as to whether the treatment might have been issued for another event.

Regarding to the age inequalities in prescribing EBPs, the results of this study were quite similar to that of Paquet *et al.*,²⁴ which demonstrated that elderly people are less commonly prescribed ACEIs and statins. However, contrary to this result, a study was conducted in China though it was subject to recall bias with small sample size of 89 patients.²² This study demonstrated that an increase in age led to increased risk of comorbidities thus reducing the opportunity of receiving recommended pharmacotherapy prescriptions due to contraindication. As much as this could be one of the hypotheses for fewer EBPs prescription for elderly patients, the results for current study were adjusted for various common associated comorbidities. Older patients were more commonly to be benefited from pharmacological treatments rather than surgical treatment, however, this age group associated with lower rate of EBPs prescription. For example, increase in age associated with lower rate of prescribing statins in patients with coronary heart disease (CHD) which has been explained as due to prescriber perception that statins are less effective or less cost effective in older patients.

Few studies have examined sex inequalities in prescribing of EBPs for patients with PAD as illustrated in table 2. Although there were several limitation surrounding the association between sex and prescribing EBPs in PAD, the most common limitation was the lack of adjustments in results.

All studies only highlighted the proportional differences in prescribing EBPs in PAD. Additionally, three of the studies presented a small sample size.²²⁻²⁴ Previous studies showed different variations in prescribing EBPs in PAD, such as antiplatelet which were prescribed more frequently in women compared to men although the variance was not significant.²¹

Klein-Weigel et al.²³ showed that prescribing of clopidogrel was significantly higher among women than in men ($P=0.03$); however, no significant differences was observed in prescribing aspirin. In contrast, men were significantly more likely to receive ACEIs than women ($p < 0.005$).²¹ Moreover, β -blockers were more commonly prescribed in men compared to women.²³ Prescribing of statins was higher among men compares to women,²¹ although the opposite was demonstrated in two small studies.^{19,20} The results of this study are the same as the previous studies to show that women received more prescriptions of statins and PVDs.

This study involved the use of SIMD score in the determination of inequalities in the prescription of EBPs between the least and most deprived patients. Notably, there were no significant variances found in the prescription of EBPs across deprivation quintiles in Scotland. This report is similar to the report of Simpson *et al.*²⁵ which showed no differences in prescribing EBPs between the least and the most deprived CHD patients. The similarity in prescribing EBPs among all deprivation quintiles may be attributed to the Scottish health care system. This provided free prescriptions to those who were on low incomes or with chronic diseases. The lower prescription costs by use of a prepayment scheme may be the reason why there was less variance in the rate of prescription across socioeconomic groups. The impact of socioeconomic status was common in countries that did not provide a free prescription of drugs for patients with chronic diseases.

As a result of the exclusion of those who died 30 days with EBPs prescription after the first diagnosis of PAD, this study is bound to selection bias. As much as selection bias may have affected the validity of these results, the number of patients excluded from this study was negligible (6.8% of 147 patients). In this regard, a higher ratio of patients who died within 30 days before EBPs prescription was identified and compared to those who died within 30 days after the first diagnosis.

In summary, prescription within 30 days differed by age, sex, except for socioeconomic status. Even though clinical trials have shown the efficacy of various EBPs in preventing events regardless of the age, elderly patients, especially those above 85-years showed less EBPs prescription. Additionally, the older patients were least likely in the risk of reducing drugs such as statins. Even though the elderly may be more likely to have multiple comorbidities, this study revealed that the age inequalities were constant even after adjustments of various commodities.

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Table 1 Baseline demographic characteristics

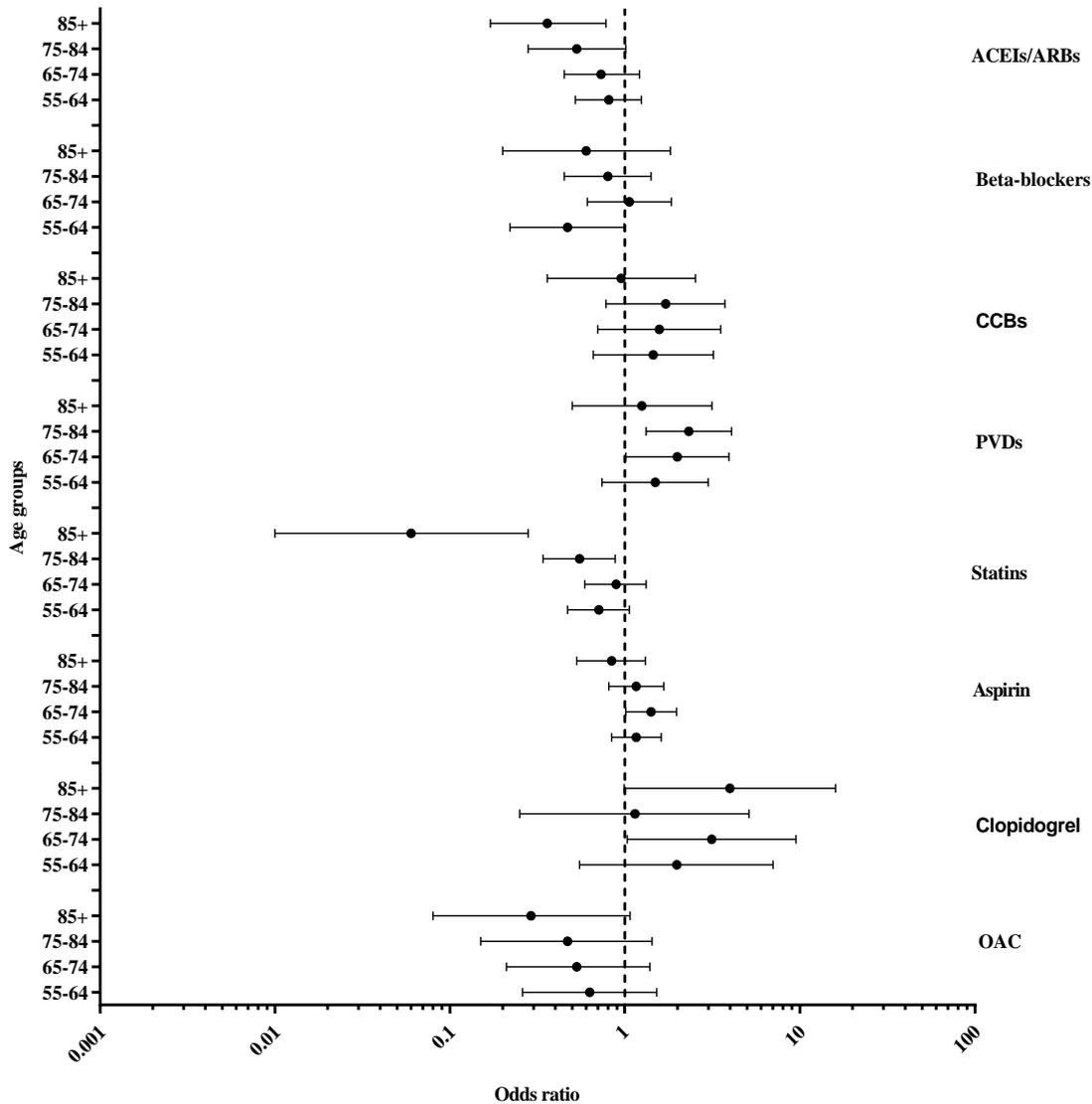
	Survived Within 30 days after 1 st diagnosis	Patients died within 30 days after 1 st	All patients (n=3532)
Male sex	1812 (53.5%)	63 (42.8%)	1875 (53.1%)
SD/variance	1.15/1.33	0.95/0.91	1.17/1.37
Age (years):			
< 55	551 (16.3%)	2 (1.4%)	553 (15.7%)
55 – 64	780 (23.0%)	9 (6.1%)	789 (22.3%)
65 – 74	1024 (30.3%)	28 (19.1%)	1052 (29.8%)
75 – 84	819 (24.2%)	56 (38.1%)	875 (24.8%)
85+	211 (6.2%)	52 (35.3%)	263 (7.4%)
Socioeconomic			
Q1 least deprived	210 (6.2 %)	6 (4.1%)	216 (6.1%)
Q2	172 (5.1%)	8 (5.4%)	180 (5.1%)
Q3	372 (10.9%)	17 (11.6%)	389 (11.0%)
Q4	249 (8.7%)	21 (14.3%)	315 (8.9%)
Q5	335 (9.9%)	11 (7.5%)	346 (9.8%)
Q6	490 (14.5%)	21 (14.3%)	511 (14.4%)
Q7	421 (12.4%)	17 (11.6%)	438 (12.4%)
Q8	345 (10.2%)	14 (9.5%)	359 (10.1%)
Q9	460 (13.6%)	21 (14.3%)	481 (13.6%)
Q1 most deprived	286 (8.5%)	11 (7.5%)	297 (8.41%)

*Only 10 (6.8%) patients died within 30 days and had a prescription, § No missing data

Study	Design/year	Reference/ subject	Prescribing	Medications	Prescribing percentage Women vs. men	OR, 95% CI Women vs. men	Adjustment	P values / statistical significance
Paquet et al²⁷	Retrospective cohort	Women=261 0 Men=3352	Post discharge within 90 days	ACEI Antiplatelet Statins	39.3 vs. 44.5 72.3 vs. 71.1 39.3 vs. 44.5	Not reported	Unadjusted	< 0.005 Not significant < 0.005
Canada								
Jing et al²⁸	Retrospective cross-sectional	N=89	Post discharge/ Diagnosis	Statins	40.0 vs. 16.0	Not reported	Unadjusted	Not reported
China	June 2007-Oct 09							
Klein-Weigel et al²⁹	Retrospective cross-sectional	Women=143 Men=121	Discharge medications documented in case records forms	ACEI ARBs Aspirin Anticoagulant β -blockers Clopidogrel	54.5 vs. 52.9 11.9 vs. 13.2 89.5 vs. 91.7 4.90 vs.	Not reported	Unadjusted	0.80 0.80 0.60 0.20 0.07 0.03
	Jan 2007-June							

Germany	2008			Statins	9.10			0.70
					33.6 vs.			
					44.6			
					74.1 vs.			
					61.2			
					72.0 vs.			
					71.2			
McDermot t et al³⁰	Randomised control trial	N=311	Not reported	LLD	73.7 vs. 79.5	Not reported	Unadjusted	Not reported
USA	Feb2006-Sep 09							

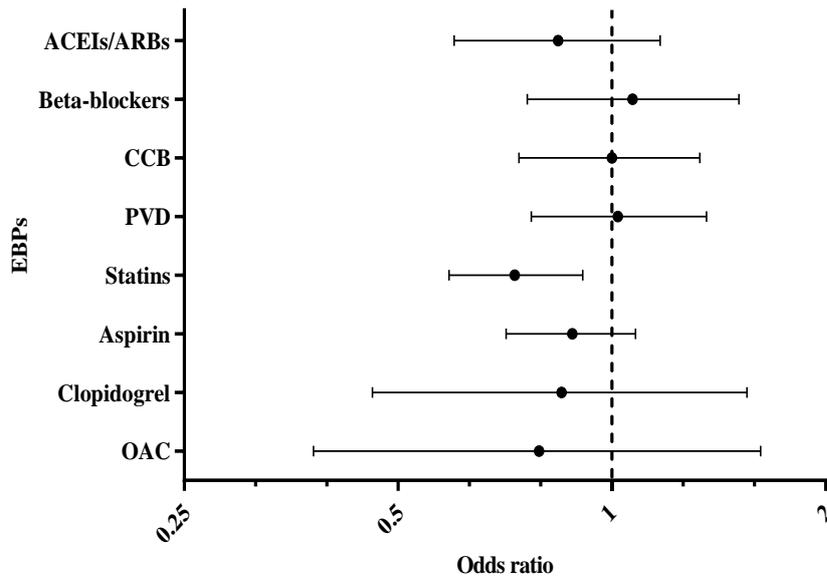
Figure 1 Odds ratio of age and prescribing EBPs within 30 days after first diagnosis of PAD.



Patients aged <55 years are the reference category. Odds ratio adjusted for sex, socioeconomic status, year of diagnosis, chronic obstructive pulmonary disease, asthma, atrial fibrillation, hypertension, diabetes, cancer, renal failure, heart failure, and stroke, CHD, clustered practices, and whether the drug was previously prescribed.

ACEI= Angiotensin converting enzyme inhibitors, ARBs= Angiotensin receptor blockers, CCB= Calcium channel blockers, OAC= Oral anticoagulants.

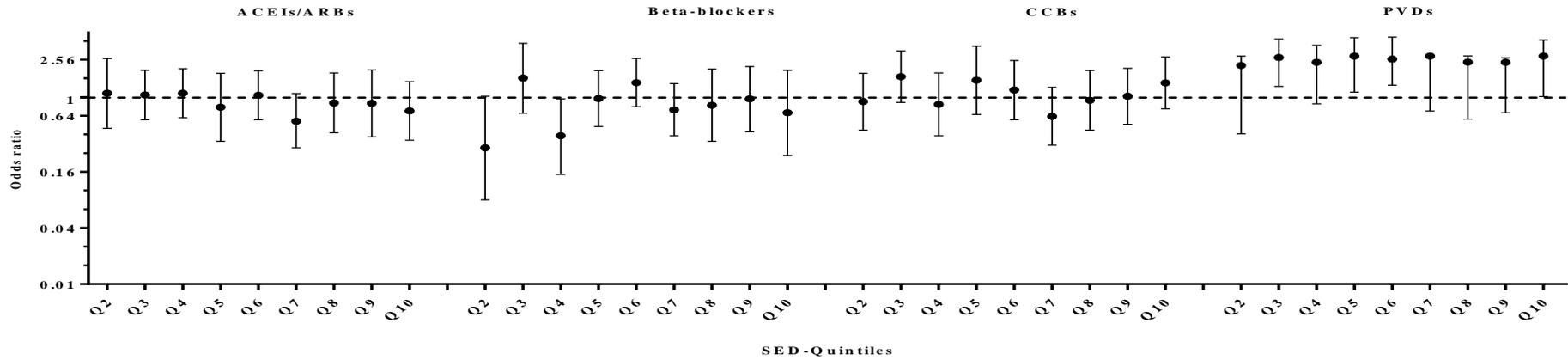
Figure 2 Odds ratio of sex and prescribing EBP's within 30 days after first diagnosis of PAD

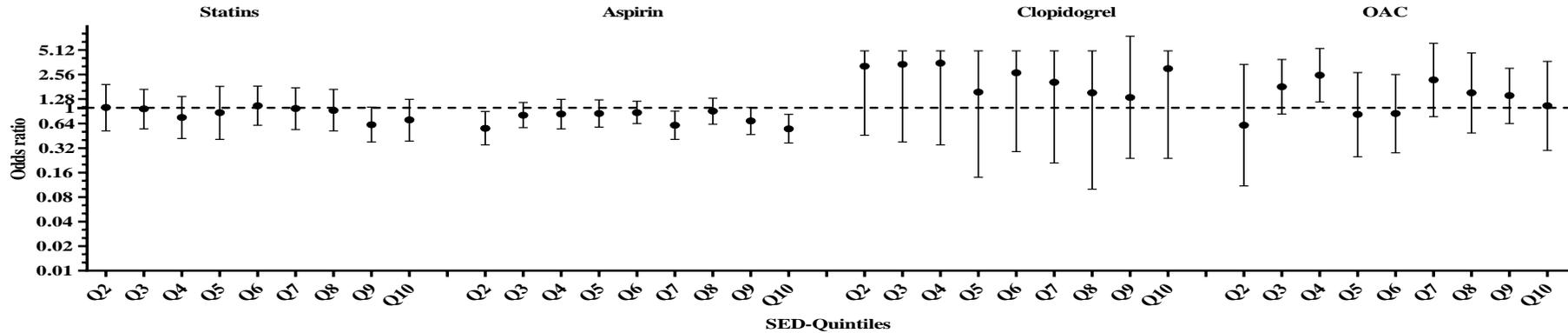


Women are the reference category. Odds ratio adjusted for age group, socioeconomic, year of diagnosis, chronic obstructive pulmonary disease, asthma, atrial fibrillation, hypertension, diabetes, cancer, renal failure, heart failure, stroke, clustered practices, and whether the drug was previously prescribed.

ACEI= Angiotensin converting enzyme inhibitors, ARBs= Angiotensin receptor blockers, CCB= Calcium channel blockers, OAC= Oral anticoagulants.

Figure 3 Odds ratio of socioeconomic deprivation and prescribing EBP within 30 days after first diagnosis of PAD





Quintile (Q1) least deprived is a reference. Odds ratio adjusted for sex, age group, year of diagnosis, chronic obstructive pulmonary disease, asthma, atrial fibrillation, hypertension, diabetes, cancer, renal failure, heart failure, and stroke, clustered practices, and whether the drug was previously prescribed. SED=Socioeconomic deprivation ACEI=Angiotensin converting enzyme inhibitors, ARBs=Angiotensin receptor blockers, CCB=Calcium channel blockers, OAC= oral anticoagulant.