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Temporal trends in the incidence, treatment patterns, and outcomes of coronary artery disease and peripheral artery disease in the United Kingdom, 2006-2015

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Abstract:	Aims: Most reports estimating national incidence rates of coronary (CAD) and peripheral arterial disease (PAD) have focused on stable outpatients or acute or elective hospital admissions, but not on the overall burden of disease. In this study, we report the changing trends in the population level incidence of CAD and PAD respectively from 2006 to 2015, statin utilisation for secondary prevention and survival outcomes using multiple nationally representative data sources from the UK (primary care encounters, hospital admissions and procedure level data).

	Methods and results: A nationally representative study of linked primary and secondary care electronic health records of 4.6 million individuals from the UK. We calculated crude and standardised annual incidence rates separately for CAD and PAD. Statin use for secondary prevention, trends in annual major vascular event rates, and mortality between 2006 and 2015, were estimated for CAD and PAD respectively. We identified 160,376 and 70,753 patients with incident CAD and PAD respectively. The age and sex-standardised incidence of CAD was similar in 2006 (443 per 100,000 person years [pyrs]) and 2015 (436 per 100,000 pyrs; adjusted incidence rate ratio [IRR] 0.98, 95%CI 0.96-1.00). By contrast, there was a 15% decline in the standardised incidence of PAD (236 per 100,000 pyrs in 2006 to 202 per 100,000 pyrs in 2015; adjusted IRR 0.85, 95%CI 0.82-0.88). The proportion of incident CAD and PAD patients prescribed long-term statins, was only 66% and 55% respectively and was less common amongst women, patients aged >70 years, with heart failure, chronic lung disease or depression. CV mortality declined by 43% for incident CAD (adjusted IRR: 0.57, 95%CI: 0.50-0.64) between 2006 and 2015 but did not decline for incident PAD (adjusted IRR: 0.84, 95%CI: 0.70-1.00). Conclusion and Relevance: In the UK, the standardised incidence of CAD appears stable but mortality rates are falling whereas the standardised incidence of PAD is falling but mortality rates are not.
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TWITTER message (Please submit a catchy Twitter message of max. 280 characters, which we would use to promote this submission in the event of acceptance - Max 280 characters).	In the last decade in the UK, the incidence of CAD appears stable but mortality rates are falling whereas the incidence of PAD is falling but mortality rates are not.
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Editor's comments

The editors have voiced interest in your manuscript, but have suggested that you in addition to the 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases as well as the 2014 ESC/EACTS Guidelines on myocardial revascularization also consider to use the 2018 ESC/EACTS Guidelines on myocardial revascularization as well as the 2016 European Guidelines on cardiovascular disease prevention in clinical practice.

Response: Thank you for this comment. We have now cited the above mentioned guidelines in the manuscript

Please see the references 16,17,42,43 (highlighted) in the manuscript

Additionally, we have now made the following changes in response to editor's comments.

1. We have now replaced "et al" in references with the full names of the authors as specified in the journal instructions page
2. ICJME Conflict of Interest Form for every author has been uploaded

Abstract

Aims: Most reports estimating national incidence rates of coronary (CAD) and peripheral arterial disease (PAD) have focused on stable outpatients or acute or elective hospital admissions, but not on the overall burden of disease. In this study, we report the changing trends in the population level incidence of CAD and PAD respectively from 2006 to 2015, statin utilisation for secondary prevention and survival outcomes using multiple nationally representative data sources from the UK (primary care encounters, hospital admissions and procedure level data).

Methods and results: A nationally representative study of linked primary and secondary care electronic health records of 4.6 million individuals from the UK. We calculated crude and standardised annual incidence rates separately for CAD and PAD. Statin use for secondary prevention, trends in annual major vascular event rates, and mortality between 2006 and 2015, were estimated for CAD and PAD respectively. We identified 160,376 and 70,753 patients with incident CAD and PAD respectively. The age and sex-standardised incidence of CAD was similar in 2006 (443 per 100,000 person years [pyrs]) and 2015 (436 per 100,000 pyrs; adjusted incidence rate ratio [IRR] 0.98, 95%CI 0.96-1.00). By contrast, there was a 15% decline in the standardised incidence of PAD (236 per 100,000 pyrs in 2006 to 202 per 100,000 pyrs in 2015; adjusted IRR 0.85, 95%CI 0.82-0.88). The proportion of incident CAD and PAD patients prescribed long-term statins, was only 66% and 55% respectively and was less common amongst women, patients aged >70 years, with heart failure, chronic lung disease or depression. CV mortality declined by 43% for incident CAD (adjusted IRR: 0.57, 95%CI: 0.50-0.64) between 2006 and 2015 but did not decline for incident PAD (adjusted IRR: 0.84, 95%CI: 0.70-1.00).

Conclusion and Relevance: In the UK, the standardised incidence of CAD appears stable but mortality rates are falling whereas the standardised incidence of PAD is falling but mortality rates are not.

Key words: Coronary artery disease, peripheral arterial disease, nationally representative electronic health records, incidence, CV outcomes, statins

Temporal trends in the incidence, treatment patterns, and outcomes of coronary artery disease and peripheral artery disease in the United Kingdom, 2006-2015

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Introduction

For the past four decades, high-income countries have experienced a tremendous decline in the standardised incidence rates of atherosclerotic cardiovascular disease (ASCVD) and cardiovascular (CV) mortality.[1–5] Nevertheless, ASCVD remains one of the leading causes of death and disability-adjusted life-years.[1,6] The age standardised prevalence of CAD in the in the UK and Europe in 2015 has been reported to be 2.5 % and 3.7% respectively. [6] The clinical spectrum of ASCVD is wide and can be broadly categorised into those involving the coronary arteries (CAD), other vascular beds (e.g., peripheral arterial disease-PAD) or both.[7,8] Estimating the population level incidence of ASCVD stratified by the involvement of vascular beds may help inform health policy, as resource utilisation and economic burden related to management may be influenced by the type of vascular beds involved.[9,10]

Most studies estimating the incidence of CAD have included either chronic ischemic heart disease from general practice (GP) consultations or acute myocardial infarction (AMI) from hospital admissions. [1,11–13] Previous studies have shown that failure to use linked primary and secondary care data can lead to a substantial (25-50%) underestimate of the burden of CAD.[14] Therefore, analyses of clinical encounters across the entire spectrum of health care services (both inpatient and outpatient) are required to capture the full burden of CAD.

Peripheral arterial disease (PAD) is reported to affect about 13% of people aged greater than 50 years in Western Europe and North America.[7,15] In spite of its high prevalence and poor prognosis, PAD attracts less attention in terms of research, early detection, and treatment. [16,17] There is a paucity of PAD data in terms of geographic and secular trends in the incidence, patient characteristics, treatment patterns, and survival.

Accordingly, we investigated the changing incidence of CAD and PAD respectively from 2006 to 2015, using multiple data sources (GP consultations, hospital admissions and procedure level data) that are representative of the UK population. We also investigated the regional variations in the incidence,

trends in cardiovascular (CV) risk factors, statin use for secondary prevention, trends in annual major vascular event rates and mortality among patients with incident CAD and PAD respectively, from 2006 to 2015.

Methods

Data source

Primary care records from general practitioners (GPs), including prescription data, caring for about 9% of the UK population were obtained from the Clinical Practice Research Datalink (CPRD) covering the period between January 1st, 1986 to December 31st, 2016.[18] Data from CPRD were linked to the hospital episode statistics (HES), which contains in-patient diagnostic and procedural records, and to the Office of National Statistics (ONS) for information on the date and cause of death.

Study population

People aged at least 18 years old with CAD or PAD were identified from CPRD using READ codes, from HES using International Classification of Diseases, tenth revision (ICD-10) codes and from Office of Population Censuses and Surveys Classification of Surgical Operations and Procedures (OPCS) revision 4.6 for codes for coronary and peripheral revascularisations (Supplementary Appendix; Tables S6). Patients with a prior diagnosis (before 1st January, 2006) of CAD or PAD (prevalent disease) were excluded for incidence calculation of CAD or PAD respectively. The incident diagnosis was defined as the first record of diagnosis in the primary care or hospital admission records. Incident cases (for both CAD and PAD) formed the base cohort for analyses of statin prescribing (Statin cohort) and HES linkage (Complications cohort) (Supplementary Figures S1 and S2)

The investigation of statin use and its predictors was restricted to patients with incident CAD and PAD aged greater than 40 years who had complete follow-up data for at least one year from the date of diagnosis. Those transferring out of a CPRD participating GP practice or whose last collection date was within a year of diagnosis were excluded (Supplementary Figure S1 and S2). Patients who could be

linked to HES and ONS (~ 60% of patients in CPRD) were used to evaluate trends in the annual rates of major vascular events and mortality between 2006 and 2015.

Patient characteristics

Common co-morbidities were identified using CPRD READ codes. READ codes used in CPRD are the standard clinical terminology system used in General Practice across the UK. READ codes gives detailed clinical coding of multiple patient features such as clinical signs, symptoms and observations; laboratory tests and results, medications and diagnoses.[18] Socioeconomic status was reported using Index of Multiple Deprivation (IMD) 2015 quintiles, with quintile 1 being the least and quintile 5 the most deprived. Information on geographic region, ethnicity, other relevant clinical variables such as body mass index and baseline medications (prior to incident diagnosis) including antiplatelet therapy, statins, angiotensin converting enzyme inhibitors or angiotensin receptor blockers (ACEI/ARB), beta-blockers, calcium channel blockers and other vasodilators were also obtained from the CPRD records.

Outcomes

The individual trends in the incidence of CAD and PAD between 2006 and 2015 were the primary outcomes of interest. The overall proportion of patients on a stable treatment regimen of statins, stratified by the type of vascular disease (CAD and PAD) and co-morbidities were described. A stable treatment regimen of statins was defined as prescriptions for more than 75% (273.75/365.25 days) of the first year after incident diagnosis. Finally, we present trends (from 2006 to 2015) in the annual age and sex adjusted event rates of complications including, myocardial infarction, stroke, hospitalisation for bleeding, CV hospitalisation (planned and unplanned), premature CV mortality (defined as death <75 years), CV mortality and all-cause mortality among patients with incident CAD and incident PAD. The complication rates were analysed only for patients whose data from CPRD could be linked to HES and ONS data-sets.

Statistical analyses

Baseline characteristics were expressed using mean ± standard deviation for continuous variables and percentages for categorical variables. Baseline characteristics were stratified by sex and three time periods of diagnosis (2006-07, 2010-11 & 2014-2015). We calculated sex and age specific (5 year intervals) incidence rates per 100,000 person years for each year. For the denominator, the total person years in each year was calculated in 5 year age intervals. Standardised incidence rates were computed individually for CAD and PAD on the basis of 2013 European standard population distribution of age and sex.[19] We employed Poisson regression models to estimate adjusted incidence rate ratios (IRR) and 95% confidence intervals (CI) for quantifying the change in the incidence rates between 2006 and 2015.

The proportion of incident CAD and incident PAD patients on statins, stratified by baseline co-morbidities were analysed. Logistic regression model was used to investigate the predictors of statin use (or non-use) after an incident diagnosis, separately for patients with incident CAD and patients with incident PAD. We adjusted the model for age, sex, year of diagnosis, and relevant co-morbidities including, diabetes mellitus (DM), hypertension (HTN), chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), depression, dementia, history of malignancy, chronic liver disease (CLD), and prior history of ischemic stroke; in addition to these, the model was also adjusted for prior history of PAD for incident CAD patients and prior history of CAD for incident PAD patients.

The event rates of complications were defined as the annual rate of occurrence (per 100 person years) of the complications during the first year of follow up. Total follow-up was calculated from the time of incident CAD or PAD diagnosis in CPRD or HES and the date of the outcome (i.e. first event for each outcome of interest), death (when it is not the outcome), date of disenrollment in the practice or of the practice in CPRD, or the end of follow up (one year from the date of incident diagnosis). Rates were age and sex standardised to 2013 European Standard Population. For all the complications, we computed adjusted IRR and 95% CI to estimate changes in the event rates over time (2006 to 2015),

separately for incident CAD and incident PAD patients. We performed sensitivity analyses for event rates and mortality in incident PAD patients by excluding those with history of concomitant CAD (Please see Supplementary Appendix for details).

Ethics approval

The study was approved by the Independent Scientific Advisory Committee of the Medicine and Healthcare Products Regulatory Agency (MHRA) for database research (protocol number: 18_057R). The data are anonymous, and the requirement for informed consent was therefore waived

Role of funding source

The present work was funded by a research grant from Bayer. VS and JKQ had full access to all the data and all authors made the final decision to publish. We had two Bayer representatives that were engaged in the project: KB and JBB. Both representatives participated to the funding of the study. KB and JBB were not involved in the data analyses and the results interpretations. No Bayer drug was involved in the study limiting risk of potential conflict of interest.

Results

From 15.4 million patient records, 4,618,735 people who were alive on Jan 1, 2006 were identified of whom 184,814 had prevalent CAD and 52,667 had prevalent PAD (Supplementary Figures S1 and S2). Between 2006 and 2015, 160,376 incident cases of CAD (base-cohort for CAD) and 70,753 incident cases of PAD (base-cohort for PAD) were identified. Using multiple data sources, compared to using primary care encounters only, we identified an additional 38,207 cases of incident CAD (25% increase) and 4,500 incident cases of PAD (7% increase) (Supplementary Figure S3).

Incidence of CAD and PAD

Across the UK, there was no change in the age- and sex-standardised incidence of CAD between 2006 and 2015 [443 per 100,000 person years in 2006 and 436 per 100,000 person years in 2015; adjusted

IRR 0.98, 95% CI 0.96 - 1.00] (Figure 1 and Take home figure). Similarly, there was no change in the crude incidence for CAD from 439 per 100,000 person years in 2006 to 450 per 100,000 person years in 2015 (IRR 1.02, 95% CI 1.00 - 1.05) (Figure 2). The age-standardised incidence of CAD was higher amongst men (650 per 100,000 person years) than women (370 per 100,000 person years) (Supplementary Figures S4 and S5). The trends in standardised incidence of CAD among men and women remained relatively stable from 2006 to 2015 (adjusted IRR for men 1.00, 95% CI 0.96 – 1.03; adjusted IRR for women 0.97, 95% CI 0.93 – 1.00) (Supplementary Figures S4 and S5). In keeping with the overall trend for CAD (which included chronic ischemic heart disease and AMI), the age- and sex-adjusted incidence rates for AMI were similar in 2006 and 2015 (adjusted IRR 0.99, 95% CI 0.95 – 1.03). We observed a transient increase in the age- and sex-standardised incidence of CAD peaking in 2008, similar to an earlier report on AMI in the UK (please see supplementary appendix for details).[11]

There was a 15% decline in the age- and sex-standardised incidence of PAD from 236 per 100,000 person years in 2006 to 202 per 100,000 person years in 2015 (adjusted IRR 0.85, 95% CI 0.82 - 0.88) (Figure 1 and Take home figure). In line with the standardised rates, there was 10% decline in the crude incidence of PAD – falling from 234 per 100,000 person years in 2006 to 211 per 100,000 person years in 2015 (IRR 0.90, 95% CI 0.87 - 0.93) (Figure 2). The decrease in the standardised incidence of PAD over time was consistent across most of the age groups. Age-standardised PAD incidence was higher in men (300 per 100,000 person years) than women (156 per 100,000 person years). Reductions in the age-standardised incidence of PAD in women from 2006 to 2015 (adjusted IRR for women 0.86, 95% CI 0.81 – 0.91) exceeded those for men (adjusted IRR for men 0.93, 95% CI 0.89 – 0.97) (Supplementary Figures S4 and S5).

Regional variations in the standardised incidence of CAD in England which were apparent in 2006, particularly the difference between the north and south, were lower in 2015 (Supplementary Figure S6). There was an overall decline in the age and sex standardised incidence of PAD, which was

substantial in some regions (e.g.:- >30% in north-west and north-east England) (Supplementary Figure S7).

Patient characteristics stratified by sex and time period

The mean age at diagnosis for CAD and PAD was similar and did not change between 2006 and 2015 (Tables 1 and 2). Patients diagnosed in more recent years were more likely to be obese, have DM, CKD, dyslipidaemia and a history of cancer. Women were slightly older and had more co-morbidities than men. The use of statins and ACE inhibitors (for primary prevention) prior to an incident diagnosis increased substantially from 2006 to 2015 in both CAD and PAD (Table 1 and Table 2).

Predictors of statin non-use for secondary prevention

We included 121,011 incident cases of CAD and 49,426 incident cases of PAD (Statin cohort) (Supplementary Figures S1 and S2). The proportion of incident cases of CAD and PAD who qualified as receiving a stable statin treatment regimen were 66% and 55% respectively. Notably, over 40% of women and 50% of elderly (age > 70 years) with established ASCVD (CAD and PAD), were not on a stable statin regimen (Table 3 and Supplementary Table S3). In a multivariable logistic regression model, for patients with CAD, failure was associated with female sex (odds ratio [OR] 0.67, 95% CI 0.65 - 0.69), heart failure (OR 0.73, 95% CI 0.69 – 0.78), age >70 years (OR 0.87, 95% CI 0.84 - 0.90), COPD (OR 0.82, 95% CI 0.78 – 0.86) and depression (OR 0.86, 95% CI 0.81 – 0.90) and was similar for PAD (Figure 3). Statin uptake did not increase significantly between 2006 and 2015 (Supplementary appendix Figure S8).

Trends in the annual event rates of major vascular events and mortality from 2006 to 2015

We included 114,807 incident cases of CAD and 45,503 incident cases of PAD (those eligible for HES-ONS linkage; Complication cohort). The overall annual age- and sex-standardised rates for MI were higher for CAD than for PAD but the reverse was true for ischemic stroke (Table 4). The age- and sex-standardised annual CV mortality was similar for CAD and PAD. However all-cause mortality was higher for PAD (9.2 per 100 person years, 95% CI 9.0-9.5) compared to incident CAD (8.2 per 100

person years, 95% CI 8.1-8.4). Age-adjusted rates of MI and bleeding requiring hospitalisation were higher in men than in women for both CAD and PAD, whereas the rate of ischemic stroke for those with incident CAD group was higher in women (Table 4 and Supplementary Table S4). Morbidity and mortality were similar for patients with PAD whether or not they had CAD (Supplementary Table S4). The annual crude incidence rates of amputation and acute limb ischemia in the overall PAD population were 2.2 (95 % CI, 2.0-2.4) and 0.6 (95 % CI, 0.5-0.7) per 100 person years of follow up respectively (Supplementary Table S5).

Comparing 2006 vs 2015, the annual age- and sex-adjusted rate of MI fell by 48% in those with incident CAD (adjusted IRR 0.52, 95% CI 0.43 - 0.63) and 56% in those with incident PAD (adjusted IRR 0.44, 95% CI 0.32 – 0.61) (Figure 4). The greatest reduction in the annual event rates of stroke were observed in incident PAD patients [PAD: adjusted IRR 0.63 (0.45 - 0.89); CAD adjusted IRR 0.84 (0.66 - 1.07)]. Between 2006 and 2015, there were no significant changes in the annual crude and adjusted rates of lower extremity amputations [crude incidence rate ratio (IRR): 1.2, 95% CI, 0.9 - 1.7; adjusted IRR: 1.2, 95% CI 0.9 – 1.7] and acute limb ischemia [crude IRR: 1.1, 95% CI, 0.3 - 3.3; adjusted IRR: 1.2, 95% CI 0.4 - 3.0] (Supplementary Table S5). A marked decline in CV mortality (43%) was observed amongst cases of incident CAD from 2006 to 2015 (adjusted IRR 0.57, 95% CI 0.50 – 0.64) which was less obvious amongst cases of incident PAD (adjusted IRR 0.86, 95% CI 0.70 – 1.00) (Figure 4), with or without concomitant CAD (Supplementary Figure S10). The rate of all-cause mortality fell amongst cases of incident CAD but rose amongst cases of PAD even after adjusting for age and sex.

Discussion

This study of a large nationally representative population in the UK over one decade provides vital insights into the trends in incidence, risk factors, statin use, major vascular complications and mortality of two important clinical spectrums of ASCVD – CAD and PAD.

In contrast to previous studies that have reported a decline until 2010, the incidence of CAD in models standardised for age and sex, in our study, has remained relatively stable between 2006 and 2015.[2,11]

The absence of a decline in CAD incidence in our study versus the findings of previous studies could have been caused by myriad reasons. Whilst improvements in primary prevention measures were expected to decrease the incidence of CAD[16], offsetting trends such as an increase in the prevalence of obesity, dyslipidaemia, diabetes and CKD may have attenuated the decline. Secondly, previous studies on the incidence of AMI included patients with prior history of chronic ischemic heart disease.[11,13,20] As result of this, some of those patients could have been on CV prevention medications, which in turn may have contributed to the decline in the incidence rates of AMI. Finally, there could have been an increase in the detection of non-ST elevation MI (NSTEMI), attributable to the introduction of high sensitivity troponin (hsTnT) as a diagnostic marker. The European Society Cardiology Study Group on Biomarkers in Cardiology recommended the routine use of hsTnT as a diagnostic biomarker for AMI in 2012,[20] possibly leading to additional identification of cases since. Data from the other European countries and the United States also have reported an increase in the incidence of NSTEMI.[22–25]

Contrary to the trends in CAD, there was a 15% reduction in the standardised incidence of PAD during the study period. The fall in the incidence rates of PAD could be due to policy measures incorporating primary prevention of ASCVD. Moreover, a significant proportion (30 - 50%) of PAD patients have CAD prior to their diagnosis[26], which could have led to an increased uptake of CV medications.

There was a notable shift in the co-morbidity burden over the last decade, especially among patients with incident PAD. Patients diagnosed with incident PAD in the more recent years (2014-15) were sicker, with a significantly higher proportion of patients with co-morbidities including obesity, DM, HLD, CKD, COPD and malignancy, compared to those diagnosed in 2006-07. In the UK National Health Service (NHS), the Quality and Outcomes Framework (QOF) introduced a pay for performance program in 2004. [27] Further changes were brought to the QOF reporting system in 2008, including the introduction of new indicators such as COPD and smoking cessation. [28] Given our study time frame begins in 2006, the 2004 QOF changes would have been assimilated in the data analysed. The rising

trends in the CV and non-CV co-morbidities from 2006-07 to 2010-11 observed in our analyses may, in part, correspond to the differences in coding practices resulting from the QOF changes in 2008. However, changes observed in the later part of the study period (from 2010-11 to 2014-15) are unlikely to be related to coding practice changes.

Our findings suggest, in spite of consistent evidence from multiple RCTs that statins reduce recurrent CV events in patients with established ASCVD, statins remain underutilized in clinical practice in the UK. A substantial segment of incident CAD (~ 1 out of every 3 CAD patients) and incident PAD (~ 1 out of every 2 PAD patients) patients were not receiving long term statin therapy. Our analyses also revealed that in addition to statins, dual and single antiplatelet therapy was also less often prescribed for those with incident PAD than those with CAD (Supplementary Figure S9). These findings are in line with the results of other large studies such as the PURE study and the SHARE study, where 30-40% of patients with established ASCVD in the developed countries were not prescribed with statin.[29–31] We observed the phenomenon of *"risk treatment paradox"* [32] in our study population i.e., ASCVD patients at higher risk (elderly, female, CHF, COPD and depression) for CV outcomes were less likely to have been prescribed persistent statin therapy by their physicians. Meta-analysis of individual data of 174,000 patients by the Cholesterol Treatment Trialists' (CTT) collaboration, showed significant reductions in recurrent CV events with statin among elderly patients with pre-existing vascular disease.[33] However, we observed an inverse relationship between treatment propensity and age with regard to statins. Among all the variables, female sex was the most significant predictor to have negatively influenced physician prescribing pattern with statins, after accounting for important confounders. Despite compelling evidence of the benefits of statin in women, [34] the reasons for the barriers in clinical practice remains unclear. Women may be more prone to statin induced myalgias, which could have led to more early discontinuations.[35] It has been shown that intense media publicity of exaggerated side effects of statins may have had a negative impact on continuation of statins, with more profound effects on women.[36,37] Our findings shine a spotlight on the necessity to highlight sex

specific disparities in the utilisation of statins in clinical practice to patients and physicians, and the imperative to implement additional sex specific strategies to improve CV outcomes for women.

Previous studies have demonstrated an increased bleeding risk after MI and PCI in women than men.[38,39] Conversely, we observed a higher age-adjusted bleeding rates requiring hospitalisation in men than women. This could be related to the higher annual age adjusted event rates of MI and subsequent use of DAPT during follow up in men (Table 4 and Supplementary Figure S9). While, these can partly explain the increased bleeding rates among men compared to women, unmeasured confounders (such as undisclosed bleeding risk etc.) might be a plausible reason for this observed difference. A single reason for this disparity is not clear from this data.

The trends in outcomes from 2006 to 2015 suggest that the reduction in the annual CV event rates and CV mortality in patients with incident CAD outpaced their PAD counterparts (even after excluding patients with concomitant CAD) (Figure 4 and Supplementary Figures S10-S13). The significant decline in recurrent CV events, recurrent CV hospitalisation and CV mortality among patients with incident CAD in the latter part of our study could be a consequence of improvements in treatment, particularly the health care policy measures related to early revascularisation in AMI. Furthermore, changes in guidelines and clinical practice, including the duration of antiplatelet therapy and the introduction of potent newer antiplatelet therapy agents (prasugrel and ticagrelor) could have influenced the adjusted incident rate ratio (2015 vs 2006) of CV outcomes (both ischemic events and bleeding).[40–43] However, this could also be related to an increase in the frequency of detecting smaller infarcts with less severity after the widespread utilisation of hsTnT. Conversely, in patients with incident PAD, there was no significant reduction in CV mortality over time. There are several potential explanations for this. Although the prevalence of smoking in the overall UK population has declined, contributing to the falling incidence of PAD, the prevalence of smoking amongst those who develop PAD has not changed over time. In addition to increasing the risk of incident PAD, cigarette smoking reduces exercise capacity and increases CV mortality among patients with prevalent PAD.[44] In the UK, a primary

care service network was established for evaluation of symptomatic PAD in primary care in 2009. However, the onset of symptoms in PAD indicates advanced systemic atherosclerosis and the effect of disease modifying CV medications might be less than what is observed in patients with CAD alone. A significant proportion of patients with PAD have established atherosclerosis in other vascular beds which could have an additive or multiplicative effect on CV mortality. However, sensitivity analyses of incident PAD patients excluding those with concomitant CAD demonstrated results comparable to the overall incident PAD patients (Supplementary Figure S10).

Strengths and limitations

Unlike previous studies, we included the entire spectrum of patients with CAD from all possible clinical encounters within the UK health system including chronic ischemic heart disease from GP encounters (READ codes), hospitalisations for AMI (HES codes) and from procedural records for coronary revascularisations (OPCS 4.6 codes). By this process, we identified an additional 38,207 incident CAD patients, a 25% increase (Supplementary Figure S3), utilizing multiple nationally representative data sources in comparison to conventional case ascertainment using one data source only.

Our study has several strengths but some limitations. While we hypothesise that the introduction of hsTnT could have led to an increase in the incidence of CAD after 2012 (due to an increase in NSTEMI cases), we were not able to perform a stratified analyses by AMI type, as ICD10 subcategory codes, do not reliably distinguish AMI type.[45] CPRD captures medications that are prescribed to patients. The fact that the patient received a prescription for a medication does not ensure that the patient actually filled or even took the medication. In addition, over-the-counter medication use or medications administered during hospitalisations were not captured. Our analyses was also restricted to the use of statin and not the dosage of statins (high potency statins) which is clinically relevant with the recent changes in guidelines. Only 60% of the CPRD patients eligible for HES and ONS linkage were included for the vascular events and mortality analyses. Another limitation of research using electronic health records includes the potential for misclassification of diseases and of the outcomes. Wherever

possible, definitions and algorithms that have been validated in these data sources were preferentially used to identify both the diseases of interest as well as complications. [46,47]

Conclusion

In conclusion, the standardised incidence of CAD appears stable but mortality rates are falling, whereas the standardised incidence of PAD is falling but mortality rates are not. The stable incidence of CAD, despite primary prevention measures, remains an important concern for healthcare policy planning for an aging population. In the general population, statin use for secondary prevention remains suboptimal and the uptake has not increased in the past decade, necessitating measures to address this gap. Our findings also highlight the importance of early identification of PAD so that disease modifying interventions (e.g., smoking cessation and statins) to improve CV outcomes can be implemented in a timely fashion.

Conflict of interest

V.S.: has none conflict of interest to declare. C.B.: has none conflict of interest to declare. R.Z.: has none conflict of interest to declare. J.H. has received personal fees from Bayer AG. A.C. has received personal fees from Bayer AG, Bristol_Myers Squibb, Daiichi-Sankyo and Pfizer; A.C. has been a consultant to Janssen and ONOP pharmaceuticals. K.B. and J.B.B. are employees of Bayer. A.B. has received honoraria/personal fees from BI, Pfizer, GSK, Novo-Nordisk, and AstraZeneca. D.S. has none conflict of interest to declare. JGFC has received honoraria/personal fees from Amgen, AstraZeneca, Bayer, Bristol-Meyer-Squibb, GSK, Medtronic, PharmaNord, Pharmacosmos, Philips, Myokardia, Torrent Pharmaceuticals, Sanofi, Vifor, Stealth Biopharmaceuticals, Servier and Novartis. S.R. has been a consultant for Takeda Pharmaceuticals, Janssen, Astra Zeneca, and Glenmark. J.K.Q. has received honoraria/personal fees from AstraZeneca, Bayer, GSK, Ins med, Chiesa and BI.

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Figure legends

Figure 1 A) Age and sex standardised incidence rates (per 100,000 person years) of CAD in the UK in 2006 vs 2015; 1 B) Age and sex standardised incidence rates (per 100,000 person years) of PAD in the UK in 2006 vs 2015

*** IRR: incidence rate ratio adjusted for age and sex; CAD: coronary artery disease; PAD: peripheral artery disease*

*** Figure 1A shows stable standardised incidence rates of CAD between 2006 and 2015; Figure 1B shows a decline in the standardised incidence of PAD between 2006 and 2015*

Figure 2 A) Number of cases stratified by age group (per total person years of follow in each age category) of CAD in the UK in 2006 vs 2015; 2 B) Number of cases stratified by age group (per total person years of follow in each age category) of PAD in the UK in 2006 vs 2015

*** IRR: incidence rate ratio adjusted for age and sex; CAD: coronary artery disease; PAD: peripheral artery disease*

*** Figure 2A shows no significant change in the crude incidence of CAD between 2006 and 2015; Figure 2B shows a decline in the crude incidence of PAD between 2006 and 2015*

Figure 3; Predictors of statin use for secondary prevention among patients with incident CAD and incident PAD

***Statin analyses was performed individually for incident CAD and incident PAD patients. The model was adjusted for age, sex, and relevant co-morbidities including, diabetes mellitus, hypertension, chronic kidney disease, chronic obstructive pulmonary disease, depression, dementia, history of malignancy, chronic liver disease, and prior history of stroke. In addition to these, the model was also adjusted for prior history of PAD for incident CAD patients and prior history of CAD for incident PAD patients.*

Figure 4; Trends in the annual age and sex adjusted event rates of major vascular events, bleeding, hospitalisation and mortality among patients with incident CAD and incident PAD in 2006 vs 2015

** *MI: Myocardial infarction, CV hospitalisation: cardiovascular hospitalisation (planned and unplanned), Premature CV death: Death <75 years of age due to cardiovascular cause, CV death: Death due to cardiovascular cause*

Take home figure: Temporal trends in the standardised incidence and CV mortality of CAD and PAD in the UK, 2006-2015

Table 1: Baseline characteristics of patients with incident CAD (2006 -2015)

	All patients	Sex		Time period		
		Male (n=91,668)	Female (n=68,708)	2006-2007 (n=28,591)	2010-2011 (n=35,287)	2014-2015 (n=25,269)
Age						
Age (years) (SD)	69·1 (13·7)	66·6 (13·2)	72·6 (13·7)	69·2 (13·5)	69·2 (13·7)	68·8 (13·8)
Age > 75 years	60,977 (38·0%)	27,232 (29·7%)	33,744 (49·1%)	11,016 (38·5%)	13,361 (37·9%)	9,407 (37·3%)
Sex						
Women	68,708 (42·8%)	N/A	N/A	12,366 (43·2%)	15,191 (43·1%)	10,530 (41·7%)
Men	91,668 (57·2%)	N/A	N/A	16,225 (56·8%)	20,096 (56·9%)	14,739 (58·3%)
Ethnicity						
White	43,298 (52·1%)	24,668 (56·9%)	18,629 (43·0%)	6,457 (14·1%)	10,141 (23·4%)	7,281 (16·8%)
Missing data	48·80%	48·80%	48·80%	59·70%	47·20%	43·70%
Socio economic quintile*						
Quintile 1	23,010 (20·0%)	13,389 (20·8%)	9,621 (19·0%)	4,319 (19·5%)	5,197 (20·4%)	3,475 (20·9%)
Quintile 2	26,128 (22·8%)	14,808 (23·1%)	11,320 (22·4%)	5,174 (23·4%)	5,842 (22·9%)	3,749 (22·6%)
Quintile 3	24,173 (21·1%)	13,574 (21·1%)	10,599 (21·0%)	4,586 (20·7%)	5,304 (20·8%)	3,483 (30·0%)
Quintile 4	22,569 (19·7%)	12,294 (19·1%)	10,275 (20·3%)	4,293 (19·4%)	4,895 (19·2%)	3,274 (19·7%)
Quintile 5 (most deprived)	18,927 (16·5%)	10,189 (15·9%)	8,738 (17·3%)	3,780 (17·1%)	4,261 (16·7%)	2,638 (15·9%)
Body Mass Index						
Mean kg/m2 (SD)	27·2 (5·9)	27·9 (5·3)	27·7 (6·5)	27·4 (5·7)	27·9 (5·9)	28·1 (6·0)
Underweight	2,710 (2·9%)	851 (1·7%)	1,859 (4·5%)	542 (3·0%)	615 (3·0%)	340 (2·6%)
Normal	27,096 (29·2%)	13,877 (26·9%)	13,218 (32·2%)	5,605 (31·2%)	5,890 (28·7%)	3,713 (28·5%)
Overweight	34,722 (37·4%)	21,615 (41·8%)	13,107 (31·9%)	6,793 (37·9%)	7,736 (37·6%)	4,748 (36·4%)
Obesity	25,054 (27·0%)	14,003 (27·1%)	11,050 (26·9%)	4,512 (25·1%)	5,562 (27·1%)	3,753 (28·8%)
Morbid obesity	3,200 (3·5%)	1,329 (2·6%)	1,871 (4·6%)	495 (2·8%)	749 (3·6%)	494 (3·8%)
Missing data	42·00%	43·00%	40·00%	37·00%	42·00%	48·00%
Smoking						
Current smoker	38,335 (23·9%)	21,323 (23·3%)	17,009 (24·8%)	6,702 (23·4%)	8,537 (24·2%)	6,051 (24·0%)
Ex-smoker	43,431 (26·5%)	27,524 (30·0%)	15,817 (23·0%)	8,565 (30·0%)	9,558 (27·1%)	5,955 (23·6%)
No	74,136 (46·2%)	40,512 (44·2%)	33,624 (48·9%)	12,742 (44·6%)	16,170 (45·8%)	12,400 (49·1%)
Missing data	4,564 (2·9%)	2,309 (2·5%)	2,255 (3·3%)	582 (2·0%)	1,023 (2·9%)	863 (3·4%)
Co-morbidities						
Diabetes Mellitus	30,611 (19·0%)	17,668 (19·3%)	12,941 (18·8%)	4,552 (15·9%)	6,658 (18·8%)	5,684 (22·5%)
Hypertension	100,037 (62·4%)	52,187 (56·9%)	47,847 (69·6%)	17,567 (61·4%)	21,812 (61·9%)	15,779 (62·4%)
Dyslipidaemia	33,358 (20·8%)	18,379 (20·0%)	14,979 (21·8%)	5,278 (18·5%)	7,451 (21·4%)	5,849 (23·1%)
Atrial fibrillation	18,398 (11·5%)	9,949 (10·9%)	8,449 (12·3%)	2,984 (10·4%)	4,023 (11·4%)	3,011 (11·9%)
Chronic Heart Failure	11,818 (7·4%)	6,218 (6·8%)	5,600 (8·2%)	2,297 (8·0%)	2,484 (7·0%)	1,851(7·3%)
Stroke	13,279 (8·3%)	6,967 (7·6%)	6,312 (9·2%)	2,033 (7·1%)	3,067 (8·7%)	2,201 (8·7%)
Peripheral arterial disease	10,810 (6·7%)	6,747 (7·4%)	4,063 (5·9%)	1,890 (6·6%)	2,499 (7·1%)	1,561 (6·2%)
Chronic Kidney Disease	26,001 (16·2%)	11,616 (12·7%)	14,385 (20·9%)	2,852 (10·0%)	6,351 (18·0%)	4,311 (17·1%)
Chronic Obstructive Pulmonary Disease	14,848 (9·3%)	8,352 (9·1%)	6,494 (9·5%)	2,431 (8·5%)	3,340 (9·5%)	2,479 (9·8%)
Depression	13,034 (8·1%)	5,966 (6·5%)	7,068 (10·3%)	2,485 (8·7%)	2,822 (8·0%)	1,952 (7·7%)
Cancer	13,715 (8·6%)	7,402 (8·1%)	6,312 (9·2%)	2,109 (7·4%)	3,164 (9·0%)	2,437 (9·6%)
High bleeding risk	12,558 (12·2%)	7,169(7·8%)	5,389 (7·8%)	2,044 (7·1%)	2,712 (7·7%)	2,173 (8·6%)
Baseline Medications						
Statins	62,571 (39·0%)	35,608 (38·8%)	26,963 (39·2%)	9,838 (34·4%)	14,265 (40·4%)	10,526 (41·7%)
At least one antiplatelet therapy	52,439 (32·7%)	28,108 (30·7%)	24,331 (35·4%)	9,871 (34·5%)	11,904 (33·7%)	7,103 (28·1%)
ACEI/ARB	60,419 (37·8%)	32,900 (35·9%)	27,518 (40·1%)	9,627 (33·7%)	13,572 (38·5%)	9,822 (38·7%)
Diuretics	49,773 (31·0%)	22,207 (24·2%)	27,566 (40·1%)	10,016 (35·0%)	10,841 (30·7%)	6,678 (26·4%)
Beta-blockers	34,567 (21·5%)	17,725 (19·3%)	16,841 (24·5%)	6,463 (22·6%)	7,366 (20·9%)	3,756 (21·9%)
Calcium channel blockers	17,911 (11·1%)	8,887 (9·7%)	9,024 (13·1%)	3,632 (12·7%)	3,916 (11·7%)	2,294 (9·1%)
Vasodilators	14,894 (9·3%)	7,708 (8·4%)	7,186 (10·5%)	3,008 (10·5%)	3,138 (8·9%)	2,121 (8·4%)

*Data available on socioeconomic status was available only for patients eligible for HES linkage n=114,807; BMI: Underweight: <18·5 kg/m2; Normal: 18·5-24·9 kg/m2, Overweight: 25-29·9 kg/m2, Obesity: 30-39·9 kg/m2, Morbid obesity: > 40 kg/m2; ACEI/ARB; Angiotensin Converting Enzyme Inhibitor/ Angiotensin Receptor Blocker

Table 2 Baseline characteristics of patients with incident PAD (2006 -2015)

	All patients	Sex		Time period		
		Male (n=42,663)	Female (n=28,090)	2006-2007 (n=15,359)	2010-2011 (n=14,812)	2014-2015 (n=11,132)
Age						
Age, mean in years (SD)	70·4 (13·8)	69·5 (12·5)	71·8 (15·5)	71·0 (13·5)	70·0 (14·0)	70·3 (13·8)
Elderly (age > 75)	30,126 (42·6%)	15,930 (37·3%)	14,196 (50·5%)	8,493 (55·3%)	6,035 (40·7%)	4,584 (41·2%)
Sex						
Women	28,090 (39·7%)	N/A	N/A	6,190 (40·3%)	5,926 (40·0%)	4,228 (38·0%)
Men	42,663 (60·3%)	N/A	N/A	9,169 (59·7%)	8,886 (60·0%)	6,904 (62·0%)
Ethnicity						
White	19,848 (57·0%)	12,105 (57·1%)	7,743 (56·4%)	3,269 (57·3%)	4,380 (57·0%)	3,527 (56·8%)
Missing data	51%	51%	51%	61%	48%	45%
Socioeconomic quintile						
Quintile 1	8,441 (18·5%)	5,059 (18·6%)	3,382 (18·4%)	1,827 (18·0%)	1,850 (19·4%)	1,219 (18·1%)
Quintile 2	10,195 (22·4%)	6,142 (22·6%)	4,053 (22·1%)	2,248 (22·1%)	2,117 (22·2%)	1,512 (22·5%)
Quintile 3	9,591 (21·0%)	5,716 (21·0%)	3,875 (21·1%)	2,085 (20·5%)	2,054 (21·5%)	1,419 (21·1%)
Quintile 4	9,537 (20·9%)	5,686 (20·9%)	3,851 (21·0%)	2,141 (21·1%)	1,901 (19·9%)	1,529 (22·7%)
Quintile 5 (most deprived)	7,815 (17·2%)	4,611 (16·9%)	3,201 (17·5%)	1,867 (18·4%)	1,618 (17·0%)	1,057 (15·7%)
Body Mass Index						
Mean, kg/m2 (SD)	26·9 (5·7)	27·1 (5·2)	26·5 (6·3)	26·6 (5·5)	26·9 (5·7)	27·4 (6·0)
Underweight	1,737 (4·1%)	643 (2·5%)	1,094 (6·4%)	376 (3·8%)	345 (3·9%)	233 (4·0%)
Normal	14,859 (34·9%)	8,382 (32·7%)	6,477 (38·1%)	3,589 (36·6%)	3,073 (34·6%)	1,863 (32·0%)
Overweight	15,321 (36·0%)	10,147 (39·6%)	5,174 (30·4%)	3,530 (36·0%)	3,190 (35·9%)	2,090 (35·9%)
Obesity	9,653 (22·7%)	5,941 (23·2%)	3,712 (21·8%)	2,124 (21·7%)	2,066 (23·3%)	1,420 (24·4%)
Morbid obesity	1,737 (4·1%)	489 (1·9%)	561 (3·3%)	191 (2·0%)	204 (2·3%)	209 (3·6%)
Missing data	40%	40%	40%	36%	40%	48%
Smoking						
Current smoker	21,835 (29·9%)	12,433 (29·1%)	8,751 (31·2%)	4,269 (27·8%)	4,708 (31·8%)	3,338 (30·0%)
Ex-smoker	19,632 (27·8%)	13,367 (31·3%)	6,265 (22·3%)	4,465 (29·1%)	4,128 (27·9%)	2,770 (24·9%)
Never smoked	129,437 (41·6%)	16,611 (38·9%)	12,826 (45·7%)	6,457 (42·0%)	5,884 (39·7%)	4,959 (44·6%)
Missing data	499 (0·7%)	251 (0·6%)	248 (0·9%)	168 (1·1%)	92 (0·6%)	65 (0·6%)
Co-morbidities						
Diabetes Mellitus	17,561 (24·8%)	11,309 (26·5%)	6,251 (22·3%)	3,389 (22·1%)	3,455 (23·3%)	3,368 (30·3%)
Hypertension	46,129 (65·2%)	27,321 (64·0%)	18,807 (67·0%)	10,164 (66·2%)	9,368 (63·2%)	7,312 (65·7%)
Dyslipidaemia	16,642 (23·5%)	10,151 (23·8%)	6,491 (23·1%)	3,211 (20·9%)	3,455 (23·3%)	2,966 (26·6%)
Atrial fibrillation	8,614 (12·2%)	5,163 (12·1%)	3,451 (12·3%)	1,718 (11·2%)	1,845 (12·5%)	1405 (12·6%)
Chronic Heart Failure	6,047 (8·5%)	3,799 (8·9%)	2,248 (8·0%)	1,480 (9·6%)	1,196 (8·1%)	939 (8·4%)
Stroke	6,353 (9·0%)	3,857 (9·0%)	2,496 (8·9%)	1,466 (9·5%)	1,318 (8·9%)	999 (9·0%)
Coronary artery disease	17,971 (25·1%)	12,521 (29·3%)	5,450 (19·4%)	4,378 (28·5%)	3,590 (24·2%)	2,534 (22·8%)
Chronic Kidney Disease	14,026 (19·8%)	7,467 (17·5%)	6,559 (23·3%)	2,147 (14·0%)	3,127 (21·1%)	2,293 (20·6%)
Chronic Obstructive Pulmonary Disease	8,582 (12·1%)	5,453 (12·8%)	3,128 (11·1%)	1,680 (10·9%)	1,757 (12·4%)	1,528 (13·7%)
Depression	5,625 (8·0%)	2,694 (6·3%)	2,930 (10·4%)	1,288 (8·3%)	1,240 (8·7%)	829 (7·4%)
Malignancy	6,791 (9·6%)	4,153 (9·7%)	2,637 (9·4%)	1,299 (8·5%)	1,480 (10·0%)	1,208 (10·9%)
High bleeding risk	5,452 (7·7%)	3,318 (7·8%)	2,134 (7·6%)	1,186 (7·7%)	1,115 (7·5%)	903 (8·1%)
Baseline Medications						
Statins	31,844 (45·0%)	20,842 (48·9%)	11,002 (39·2%)	6,399 (41·2%)	6,668 (45·0%)	5,337 (47·9%)
At least one antiplatelet therapy	27,059 (38·2%)	17,296 (40·5%)	9,763 (34·8%)	6,396 (41·7%)	5,593 (37·8%)	3,802 (34·2%)
ACEI/ARB	30,241 (42·7%)	18,664 (43·7%)	11,337 (40·4%)	6,313 (41·1%)	6,269 (42·3%)	4,817 (43·3%)
Diuretics	23,610 (33·4%)	12,413 (29·1%)	11,197 (39·9%)	6,033 (39·3%)	4,663 (31·5%)	3,204 (28·9%)
Beta-blockers	18,421 (26·0%)	11,460 (26·7%)	6,961 (24·8%)	4,156 (27·1%)	3,734 (25·2%)	2,909 (26·1%)
Calcium channel blockers	8,629 (12·2%)	5,112 (12·0%)	3,517 (12·5%)	2,303 (15·0%)	1,698 (11·5%)	1,050 (9·4%)

Vasodilators	8,721 (12·3%)	5,410 (12·7%)	3,311 (11·8%)	2,320 (15·1%)	1,672 (11·3%)	1,159 (10·4%)

**Data available on socioeconomic status was available only for patients eligible for HES linkage n=114,807; BMI: Underweight: <18·5 kg/m2; Normal: 18·5-24·9 kg/m2, Overweight: 25-29·9 kg/m2, Obesity: 30-39·9 kg/m2, Morbid obesity: > 40 kg/m2*; *ACEI/ARB; Angiotensin Converting Enzyme Inhibitor/ Angiotensin Receptor Blocker*

Table 3

Table3: Baseline characteristics of CAD and PAD patients with and without statins

	Statin prescriptions (CAD)		Statin prescriptions (PAD)	
	Yes (n=79,641)	**No (n=41,370)**	**Yes (n=27,150)**	**No (n=22,276)**
Age (years), mean (SD)	***67·3(11·6)***	***69·2(13·5)***	***70·7 (10·1)***	***70·4 (12·5)***
Age 40-49 years	5,590 (7·0%)	3,789 (9·2%)	664 (2·4%)	1,228 (5·5%)
Age 50-59 years	15,170 (19·0%)	7,031 (17·0%)	3170 (11·7%)	3,496 (15·7%)
Age 60-69 years	23,800 (29·9%)	9,474 (22·9%)	7,989 (29·4%)	5,480 (24·6%)
Age 70-79 years	22,254 (27·9%)	10,295 (24·9%)	9,716 (35·8%)	5,995 (26·9%)
Age > 80 years	12,820 (16·1%)	10,873 (26·3%)	5,611 (20·7%)	6,077 (27·3%)
Sex				
Women	29,687 (37·3%)	20,713 (50·1%)	9,143 (33·7%)	9,086 (40·8%)
Men	49,960 (62·7%)	20,744 (50·1%)	18,007 (66·3%)	13,189 (59·2%)
Socioeconomic quintile				
Quintile 1	10,873 (21·4%)	6,009 (19·5%)	3,001 (18·4%)	2,490 (18·2%)
Quintile 2	11,776 (23·2%)	6,874 (22·3%)	3,665 (22·4%)	3,001 (22·0%)
Quintile 3	10,459 (20·6%)	6,711 (21·8%)	3,315 (20·4%)	2,926 (21·4%)
Quintile 4	9,670 (19·2%)	6,132 (19·9%)	3,523 (21·6%)	2,913 (21·3%)
Quintile 5	8,053 (15·8%)	5,111 (16·6%)	2,796 (17·2%)	2,322 (17·0%)
Smoking				
Current smoker	19,946 (25·7%)	9,993 (24·7%)	8,265 (30·4%)	7,713 (34·6%)
Co-morbidities				
Diabetes Mellitus	16,276 (20·4%)	6,076 (14·7%)	8,578 (31·6%)	4,108 (18·4%)
Hypertension	48,789 (61·3%)	24,748 (59·8%)	20,553 (75·7%)	12,768 (57·3%)
Prior acute coronary syndrome	29,660 (37·2%)	6,104 (14·8%)	4,906 (18·1%)	1,613 (7·2%)
Stroke	6,179 (7·8%)	2,997 (7·2%)	2,824 (10·4%)	1,305 (5·9%)
*h/o Peripheral artery disease	5,418 (6·8%)	2,327 (5·6%)	N/A	N/A
*h/o Coronary artery disease	N/A	N/A	9,641 (35·5%)	3,598 (16·1%)
Chronic Kidney Disease	10,760 (13·5%)	6,428 (15·5%)	5,603 (20·6%)	3,617 (16·2%)
Heart Failure	4,143 (5·2%)	3,418 (8·3%)	2,289 (8·2%)	1,454 (6·5%)
Dementia	2,296 (2·9%)	1,610 (3·9%)	1,035 (3·8%)	806 (3·6%)
COPD	6,221 (7·8%)	4,132 (10·0%)	3,318 (12·2%)	2,882 (12·9%)
Chronic Liver Disease	880 (1·1%)	647 (1·6%)	348 (1·2%)	383 (1·7%)
Depression	6,071 (7·6%)	3,754 (9·1%)	2,088 (7·7%)	1,782 (8·0%)
Malignancy	5,610 (7·0%)	3,635 (8·8%)	2,326 (8·6%)	2,106 (9·5%)
Management				
Mean number of medications during follow up, mean (SD)	5·5 (4·0)	5·4 (4·1)	5·9 (4·4)	5·6 (4·3)

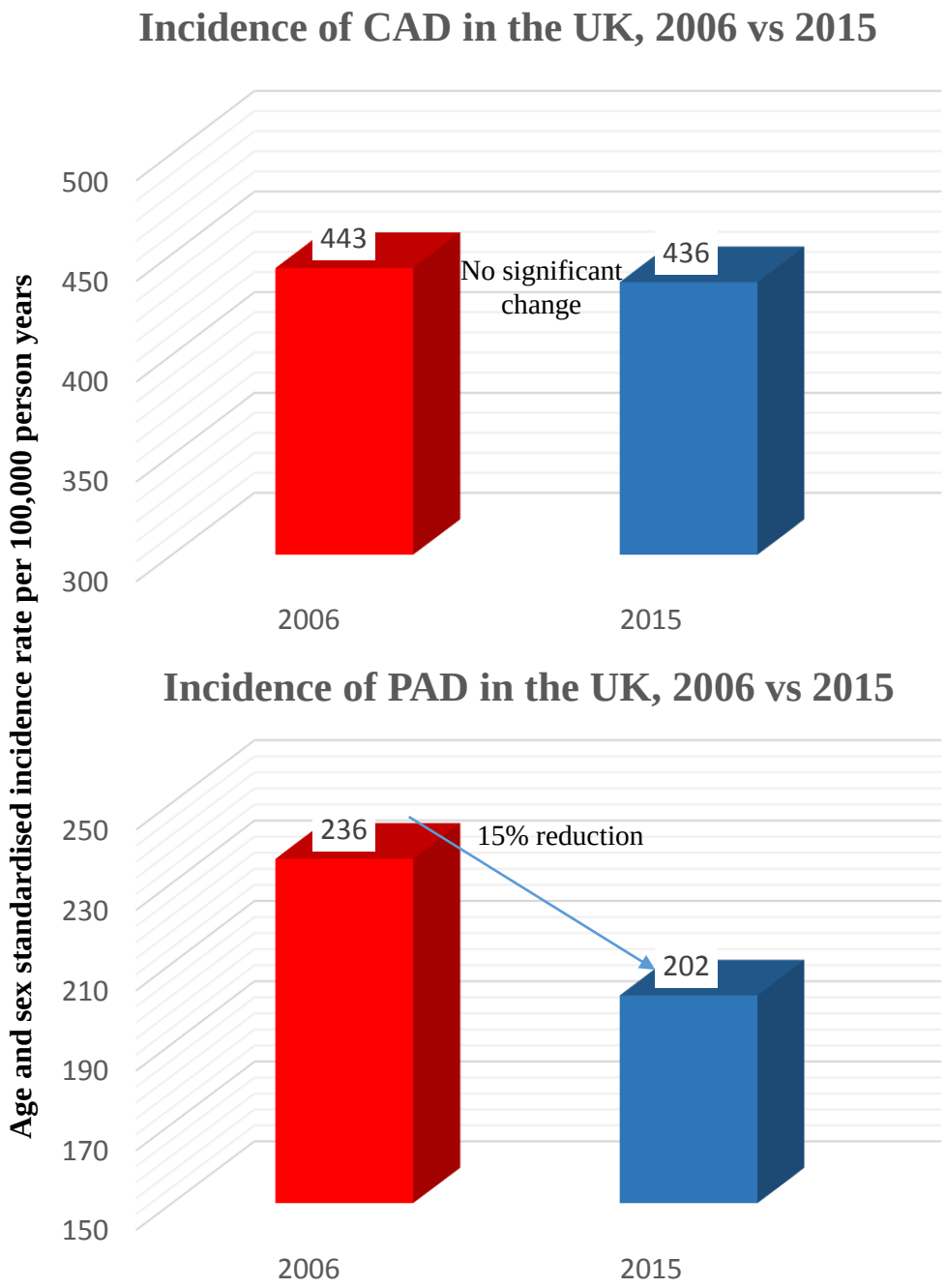
*h/o: history of; *the model was also adjusted for prior history of PAD for incident CAD patients and prior history of CAD for incident PAD patient; COPD: Chronic obstructive pulmonary disease.

Table 4 Complications of patients with incident CAD and PAD

	Annual crude incidence rate per 100-person years, 95% CI	Standardized annual incidence rate per 100-person years, 95% CI		
		Age and sex standardized	Male (age standardized)	Female (age standardized)
Incident CAD				
MI	3·1 (3·0 - 3·2)	2·4 (2·3 - 2·5)	2·8 (2·6 - 2·9)	1·7 (1·6 - 1·8)
Ischemic Stroke	2·1 (2·0 - 2·2)	1·4 (1·3 - 1·4)	1·2 (1·1 - 1·3)	1·6 (1·5 - 1·7)
Hospitalization for bleeding	2·5 (2·4 - 2·6)	1·7 (1·6 - 1·8)	1·9 (1·8 - 2·0)	1·5 (1·4 - 1·6)
CV hospitalization	11·8 (11·6 - 12·0)	9·7 (9·5 - 9·9)	10·1 (9·8 - 10·4)	9·1 (8·8 - 9·3)
Premature CV death	2·2 (2·1 - 2·4)	2·0 (1·9 - 2·1)	2·2 (2·1 - 2·3)	1·7 (1·5 - 1·8)
Premature death from any cause	6·1 (5·9 - 6·3)	4·5 (4·4 - 4·6)	4·5 (4·4 - 4·6)	4·4 (4·2 - 4·7)
CV death	7·8 (7·6 - 8·0)	3·7 (3·6 - 3·8)	3·8 (3·7 - 3·9)	3·5 (3·4 - 3·6)
Death from any cause	17·1 (16·8 - 17·4)	8·2 (8·1 - 8·4)	8·3 (8·1 - 8·4)	8·2 (8·0 - 8·4)
Incident PAD				
MI	2·9 (2·7 - 3·1)	1·9 (1·8 - 2·0)	2·3 (2·1 - 2·4)	1·4 (1·3 - 1·5)
Ischemic Stroke	2·6 (2·4 - 2·7)	1·6 (1·5 - 1·7)	1·7 (1·5 - 1·8)	1·4 (1·3 - 1·6)
Hospitalization for bleeding	2·1 (2·0 - 2·3)	1·4 (1·3 - 1·5)	1·6 (1·4 - 1·7)	1·2 (1·1 - 1·2)
CV hospitalization	10·3 (10·0 - 10·6)	6·6 (6·4 - 6·7)	7·8 (7·5 - 8·1)	4·9 (4·7 - 5·2)
Premature CV death	2·5 (2·3 - 2·8)	2·1 (1·9 - 2·3)	2·3 (2·1 - 2·5)	1·9 (1·6 - 2·1)
Premature death from any cause	8·3 (8·0 - 8·7)	6·2 (5·8 - 6·4)	7·3 (6·9 - 7·8)	7·2 (6·5 - 7·9)
CV death	7·6 (7·3 - 7·8)	3·5 (3·3 -3·6)	3·7 (3·5 - 3·9)	3·5 (3·3 - 3·6)
Death from any cause	18·5 (18·1 - 18·9)	9·2 (9·0 - 9·5)	9·1 (8·7 - 9·4)	9·6 (9·3 - 9·9)

MI: Myocardial infarction, CV hospitalization: cardiovascular hospitalization (planned and unplanned), Premature CV death: Death <75 years of age due to cardiovascular cause, CV death: Death due to cardiovascular cause

Take home figure



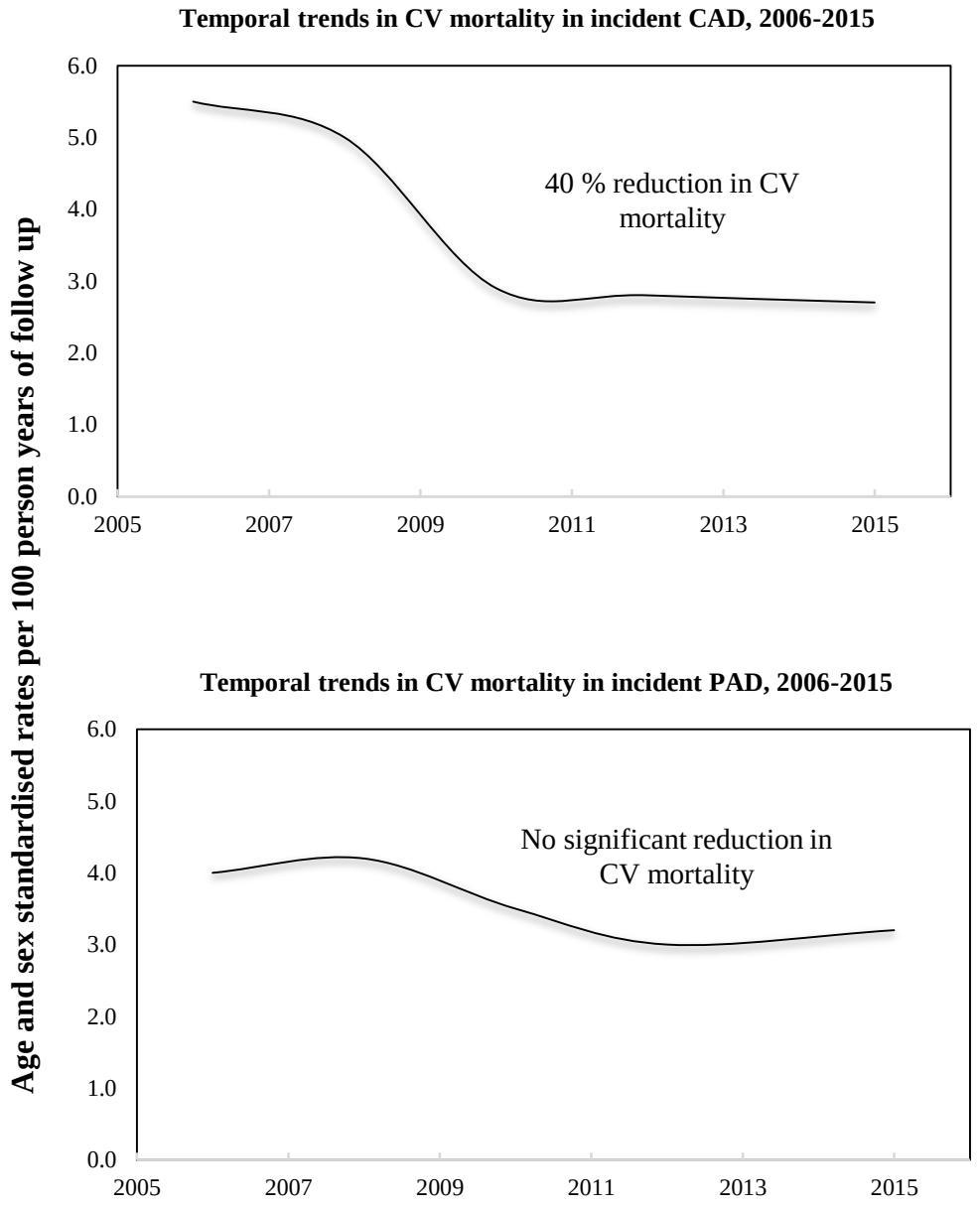


Figure 1

Figure 1

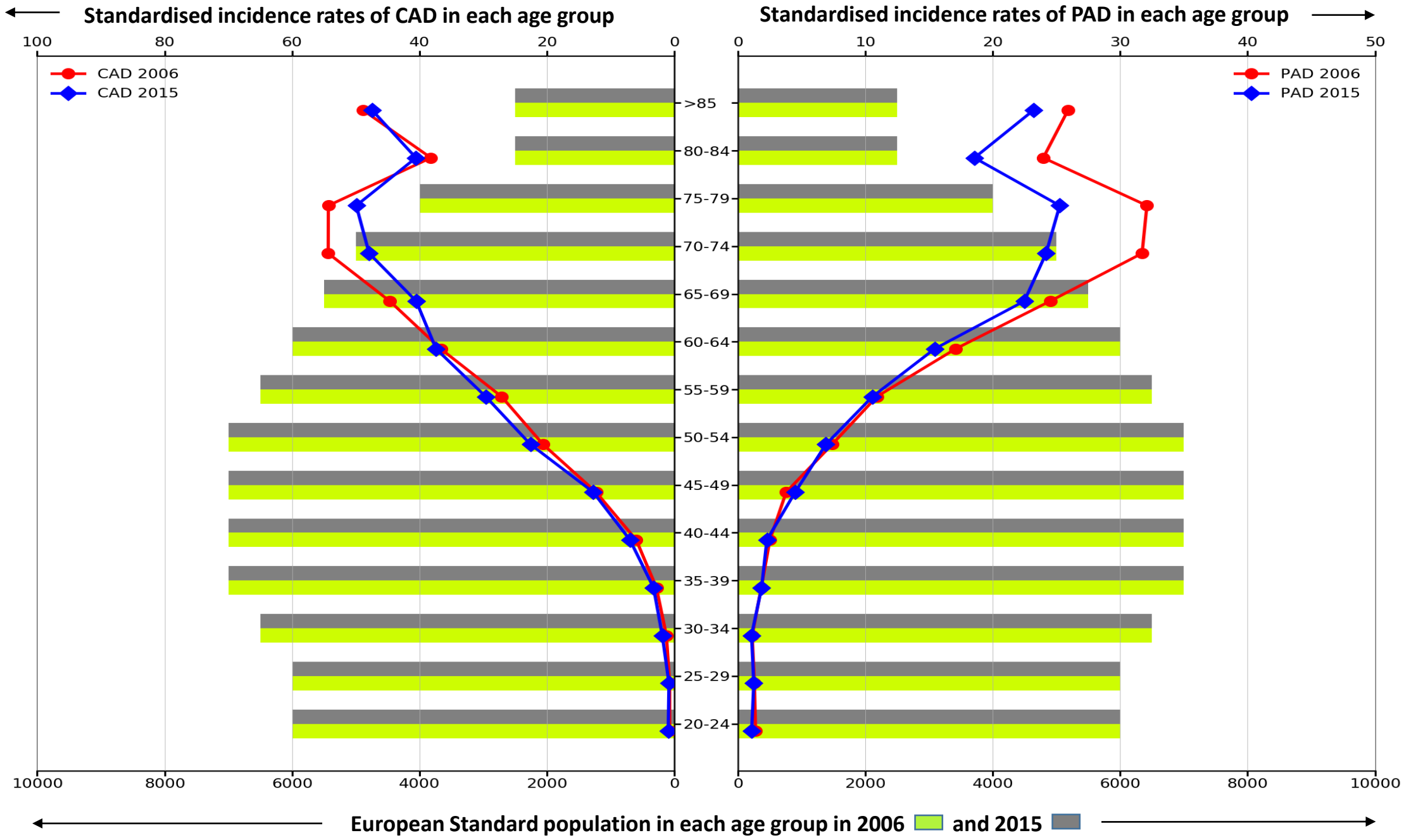


Figure 2

Figure 2

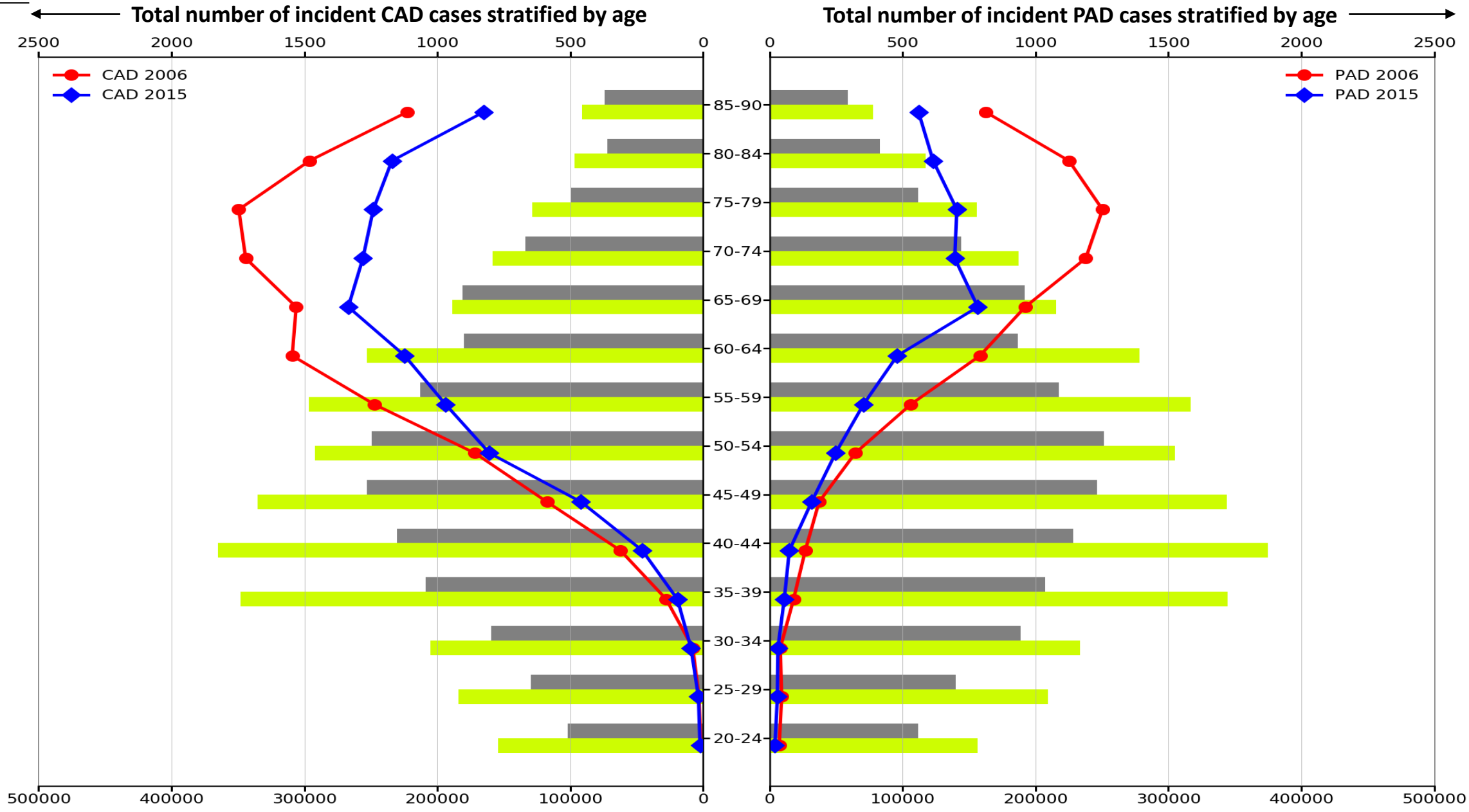


Figure 3

Figure 3; Predictors of statin use for secondary prevention among patients with incident CAD and incident PAD

Patient characteristic	Number of patients on statin/Total number of patients, %	Adjusted Odds ratio (95% CI)
Women	29,681/50,394 (59%) 10,805/18,229 (57%)	0·67 (0·65 - 0·69) 0·78 (0·76 - 0·80)
Heart Failure	4,143/7,561 (55%) 2,229/3,683 (61%)	0·73 (0·69 - 0·78) 0·80 (0·72 - 0·88)
Age >70 years	35,281/56,249 (62%) 15,320/27,399 (55%)	0·87 (0·84 - 0·90) 0·89 (0·85 - 0·94)
COPD	10,353/10,355 (60%) 3,318/6,200 (54%)	0·82 (0·78 - 0·86) 0·94 (0·87 - 1·01)
h/o malignancy	5,610/9,245 (61%) 2,326/4,432 (53%)	0·85 (0·80 - 0·90) 0·84 (0·77 - 0·91)
Depression	6,071/9,825 (62%) 2,088/3,870 (54%)	0·86 (0·81 - 0·90) 0·94 (0·86 - 1·03)
Chronic kidney disease	10,768/17,188 (63%) 5,603/9,220 (61%)	0·96 (0·92 - 1·00) 0·99 (0·93 - 1·06)
Peripheral arterial disease/ Coronary artery disease	5,418/7,745 (70%) 9,641/13,239 (73%)	1·35 (1·26 - 1·44) 2·04 (1·90 - 2·20)
Hypertension	48,789/73,537 (67%) 20,553/33,321 (62%)	1·40 (1·35 - 1·45) 1·77 (1·67 - 1·87)
Diabetes Mellitus	16,276/22,352 (73%) 8,578/12,686 (68%)	1·63 (1·57 - 1·70) 1·70 (1·62 - 1·81)

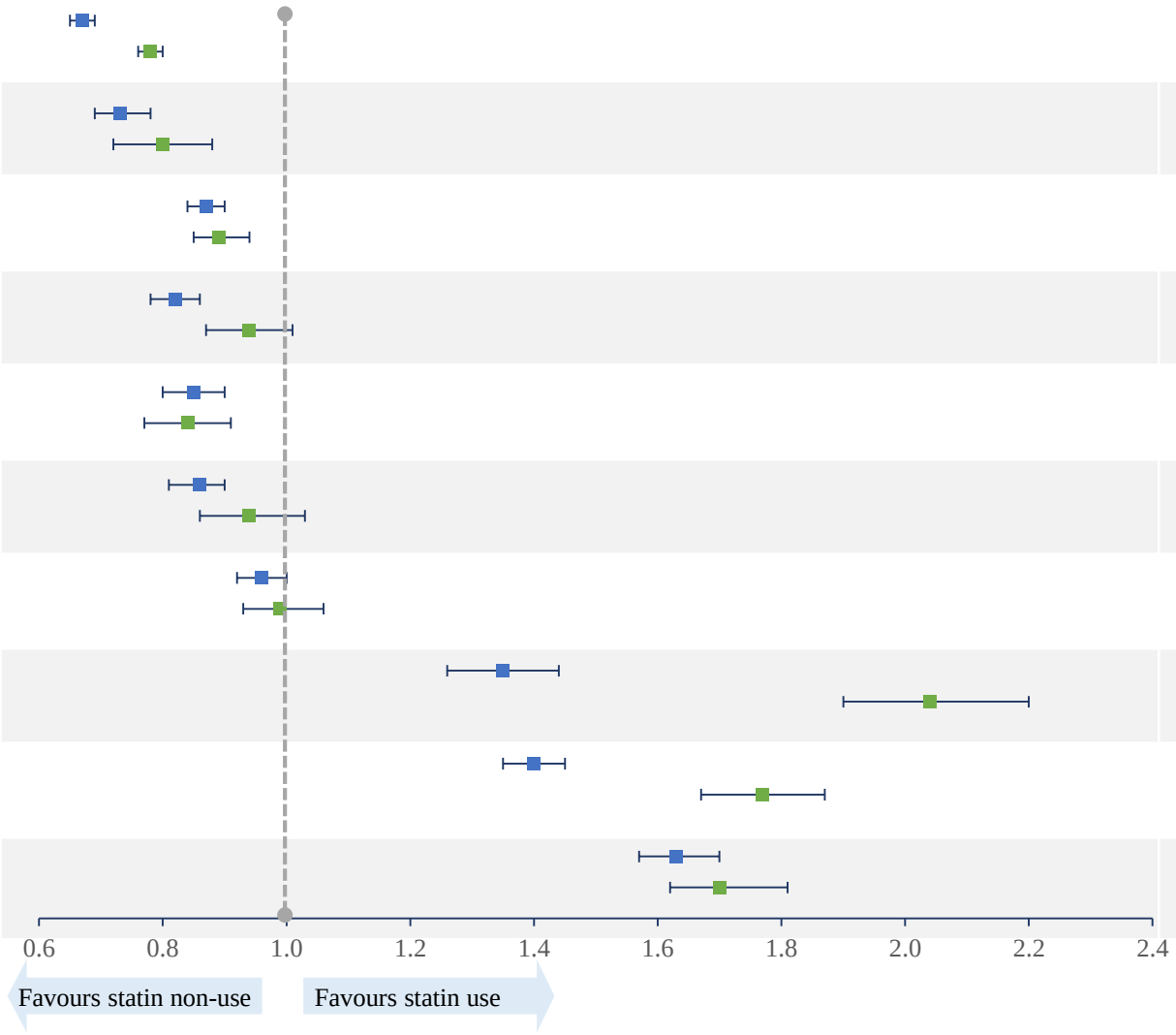
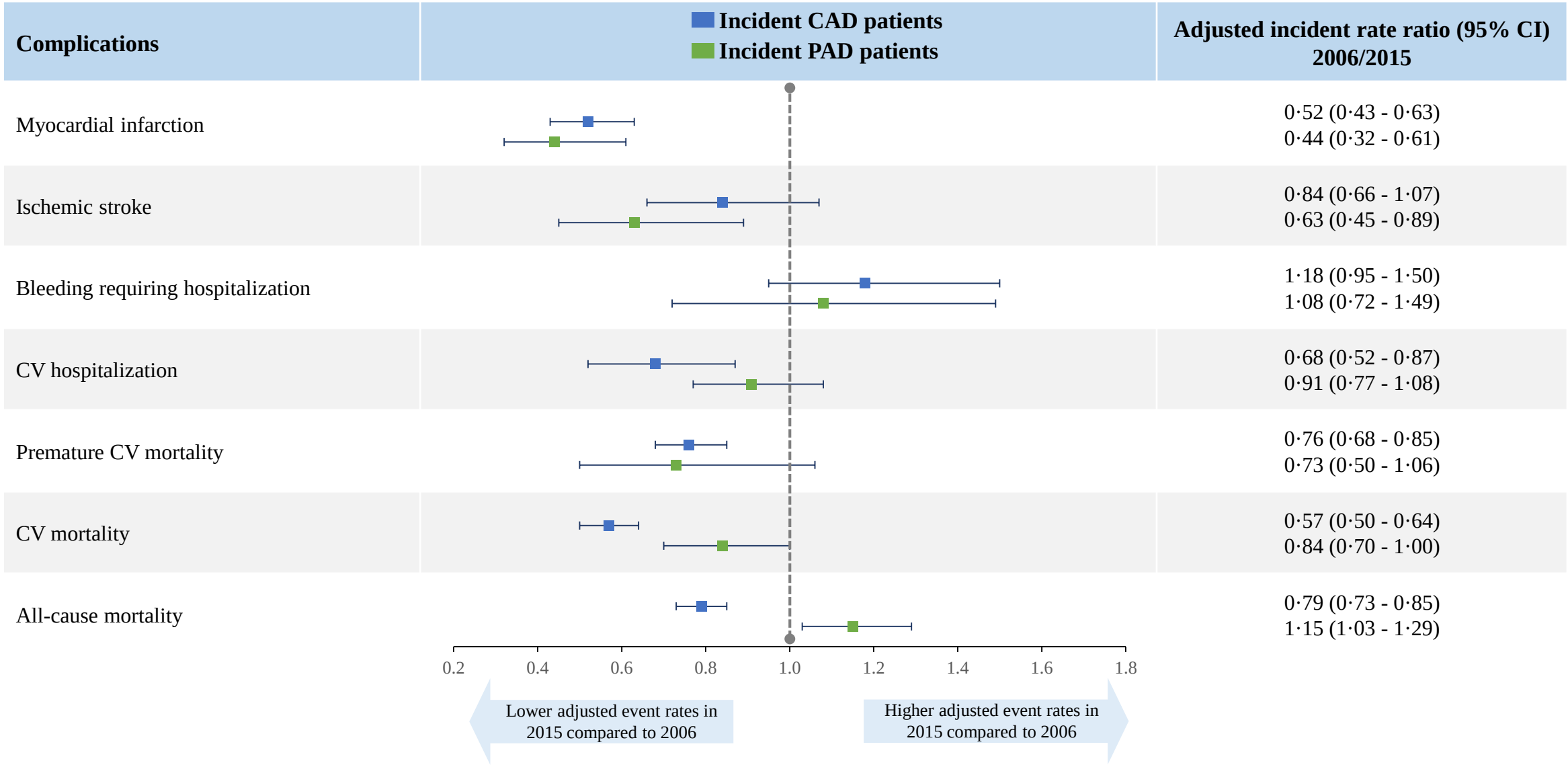


Figure 4

Figure 4; Trends in the annual age and sex adjusted event rates of major vascular events, bleeding, hospitalization and mortality among patients with incident CAD and incident PAD in 2006 vs 2015



SUPPLEMENTARY APPENDIX

Contents

Participating Investigators

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Study population: Data-source

Clinical Practice Research Data-link (CPRD):

CPRD is jointly funded by the National Health Service (NHS), National Institute for Health Research (NIHR) and the Medicines and Healthcare Products Regulatory Agency (MHRA). CPRD includes around 670 primary care practices representing around 9% of the UK population. [1]

Hospital Episode Statistics (HES)/ Office of National Statistics (ONS):

Hospital Episode statistics (HES) is an inpatient database, which contains information of all hospitalisations, inpatient procedures, hospital outpatient appointments and accident and emergency attendances at National Health Service (NHS) hospitals in England and about all patients admitted to National Health Service (NHS) hospitals in England. Each patient encounter in the hospital contains up to 20 diagnosis fields coded according to ICD-10. [2] The Office for National Statistics (ONS) is the recognized national statistical institute and is largest independent producer of official statistics in the UK. It is responsible for collecting and publishing statistics related to the population at national, regional and local levels. It conducts the census in England and Wales every ten years. CPRD and HES are linked to the Office of National Statistics using each patient's unique National Health Service (NHS) number and provides information on the place and cause of death.[3]

Identification of cases:

All patients with CAD codes from CPRD practicing GP practices were extracted. Following this, all patients with CAD codes (acute myocardial infarction and revascularisation for CAD) were extracted from HES. A unique anonymized identifier was used to link the two datasets (CPRD and HES), and the Office for National Statistics mortality data. The incident diagnosis was defined as the first record of diagnosis in the primary care (CPRD) or hospital admission records (HES). Similar extraction process was followed for identification of incident PAD patients, thereby avoiding duplication of incident cases.

Detailed description of methods

The incidence cohort consisted of patients meeting the following inclusion criteria from January 1st, 2006 onward; aged ≥ 18 years, registered at their general practice for ≥ 1 year, registered at a practice that has been submitting data that meet data quality standards for continuity and plausibility of data recording for ≥ 1 year. The requirement that patients be registered at their general practice for ≥ 1 year was meant to ensure that patient's comorbidity burden can be adequately described because patients are followed within the practice. The requirement that the patient be treated at a practice submitting data meeting a set of quality standard for ≥ 1 year was meant to ensure that the results of the study are valid and reliable.

The incidence rate of CAD and PAD was estimated yearly and over the study period (2006-2015). To calculate the incidence rate of CAD and PAD we considered incident or "new" diagnoses. A patient with incident CAD or PAD was only counted once over the study period. A diagnosis was considered to be incident if the patient did not have a diagnosis (in CPRD or HES) or undergo a procedure used to treat CAD or PAD prior to January 1, 2006 (data was available from 1985). For example, to be considered to have incident CAD, the patient should not have a diagnosis of CAD or have undergone coronary artery bypass grafting or percutaneous coronary intervention.

Statin use was identified by outpatient pharmacy prescription fills using product codes. Statins included atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, and simvastatin.

Sensitivity analyses For incidence calculations of CAD, we performed sensitivity analysis by expanding the diagnosis codes which were not specific for incident diagnosis (e.g. CAD monitoring first letter, CAD monitoring second letter etc.). We also performed sensitivity analyses for annual event rates of major vascular events, CV mortality and all-cause mortality in incident PAD patients by excluding those with prior history of CAD.

Statistical analyses were performed using STATA software, version 14.2.

Ethics approval

The study was approved by the Independent Scientific Advisory Committee of the Medicine and Healthcare Products Regulatory Agency (MHRA) for database research (protocol number: 18_057R).

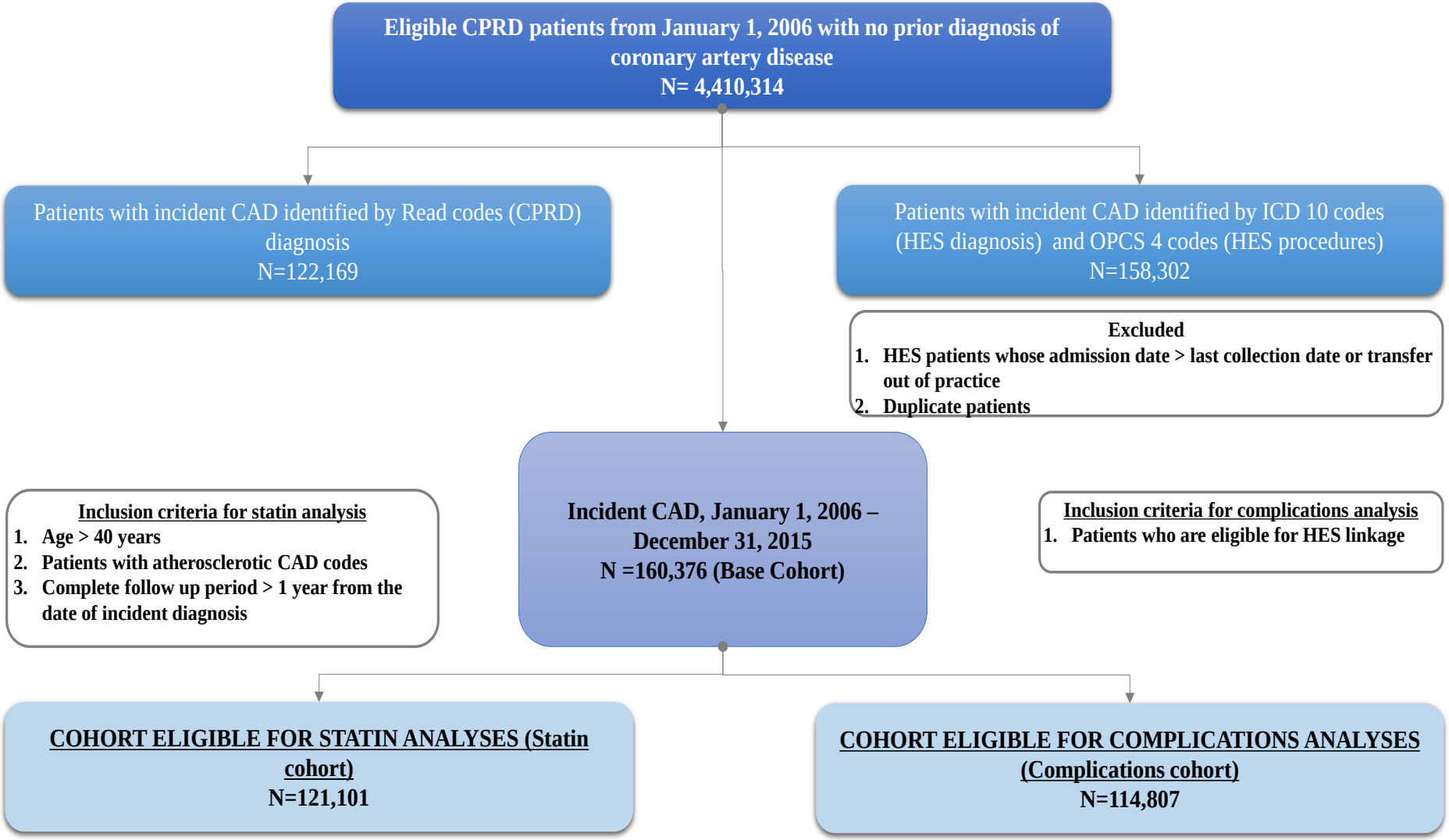
Results:

We observed a transient increase in the incidence of CAD between 2008 and 2010 (standardised incidence peaked 560 per 100,000 person years in 2008), similar to the earlier studies on the incidence of acute myocardial infarction in the UK.[4] While the reasons for this transient increase is unclear, it was thought to be related to the financial crisis as there was a disproportionate increase in the incidence of acute myocardial infarction in the London area.[4] In 2004 the UK National Health Service introduced the largest health related pay-for- performance scheme in the world—the Quality and Outcomes Framework (QOF). In 2008/09, significant changes were made in QOF with the introduction of two new indicators.[5, 6] These changes could have led to modifications in the coding pattern in the UK. However, sensitivity analyses including certain CAD codes (medcode 25814: coronary heart disease monitoring first letter, medcode 34207: coronary heart disease monitoring second letter; medcode 34329: medcode 34207: coronary heart disease monitoring third letter) showed trends in the standardised incidence rates which were comparable to the overall analyses. (404 per 100,000 person years in 2006, peaking at 576 per 100,000 person years in 2008 and back to 417 per 100,000 person years in 2015).

Sensitivity analyses was performed in incident PAD patients by excluding those with a prior history of CAD (n=34,283 with HES linkage). The annual event rates of major vascular complications, including AMI, stroke and bleeding, CV mortality and all-cause mortality, in this group were similar to the overall incident PAD patients (Supplementary table S3). Comparing 2006 vs 2015, the annual age and sex adjusted incident rate ratio for major vascular event rates, CV mortality and all-cause mortality in the

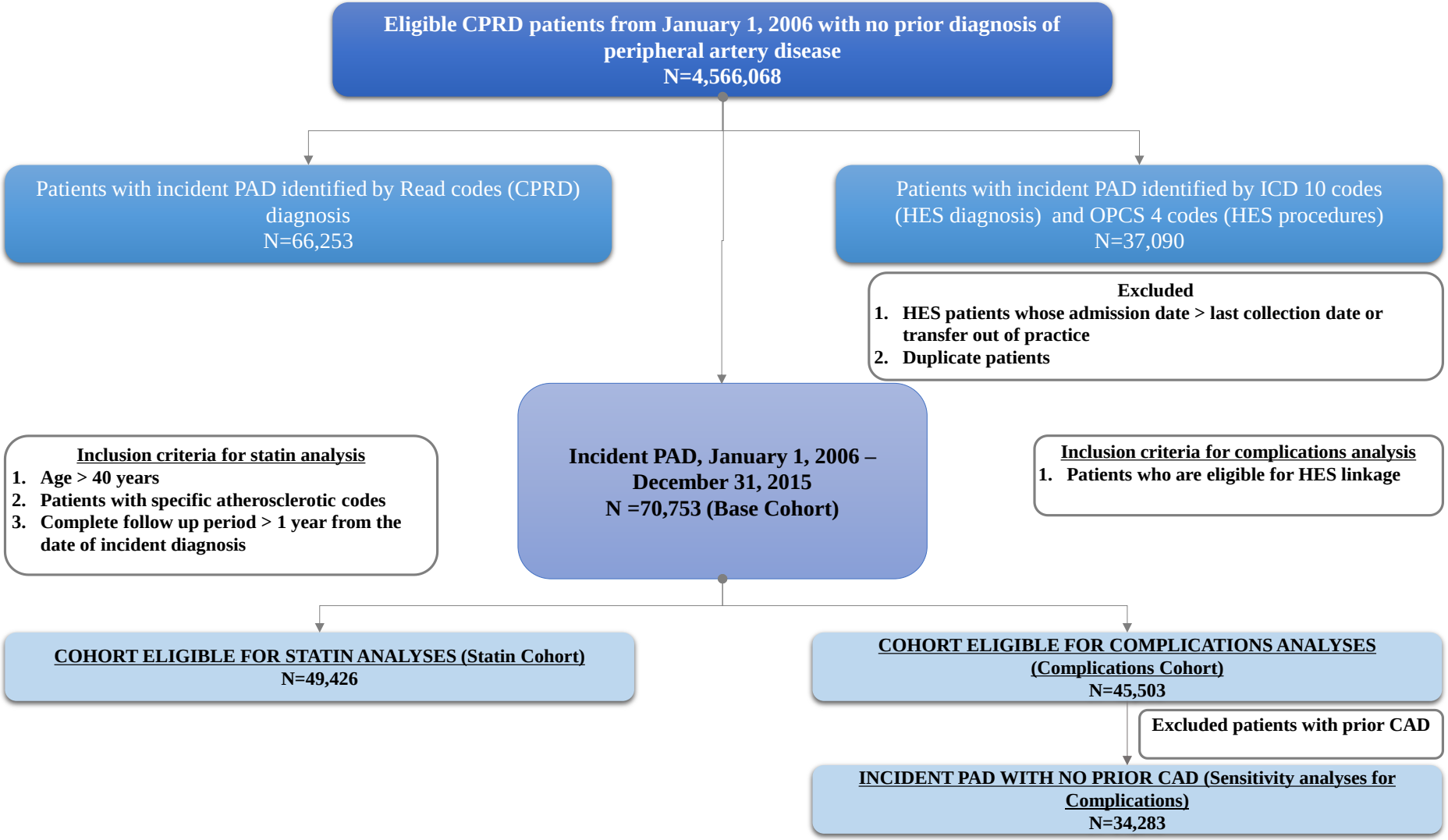
incident PAD patients with no history of prior CAD were similar to the overall incident PAD patients (Supplementary Figure S8)

Supplementary Figure S1: Flow chart for identification of patients with incident coronary artery disease: 2006-2015



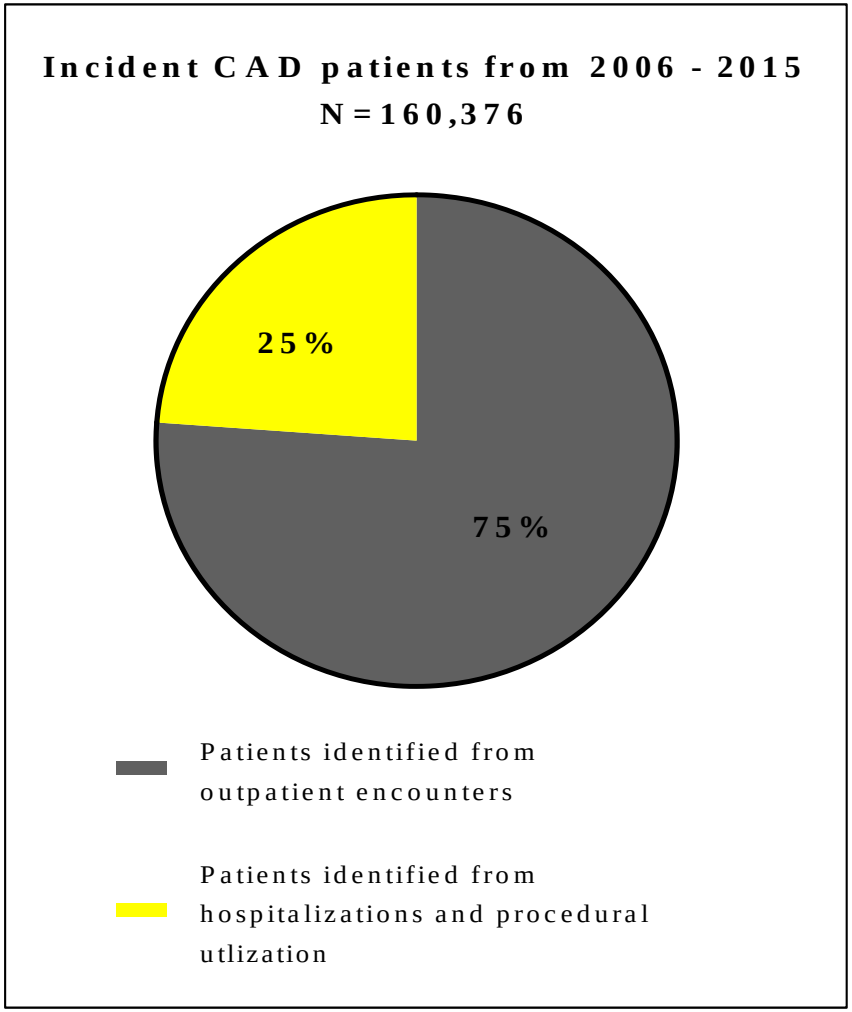
CAD: Coronary artery disease; CPRD: Clinical Practice Research Datalink; HES: Hospital Episode Statistics

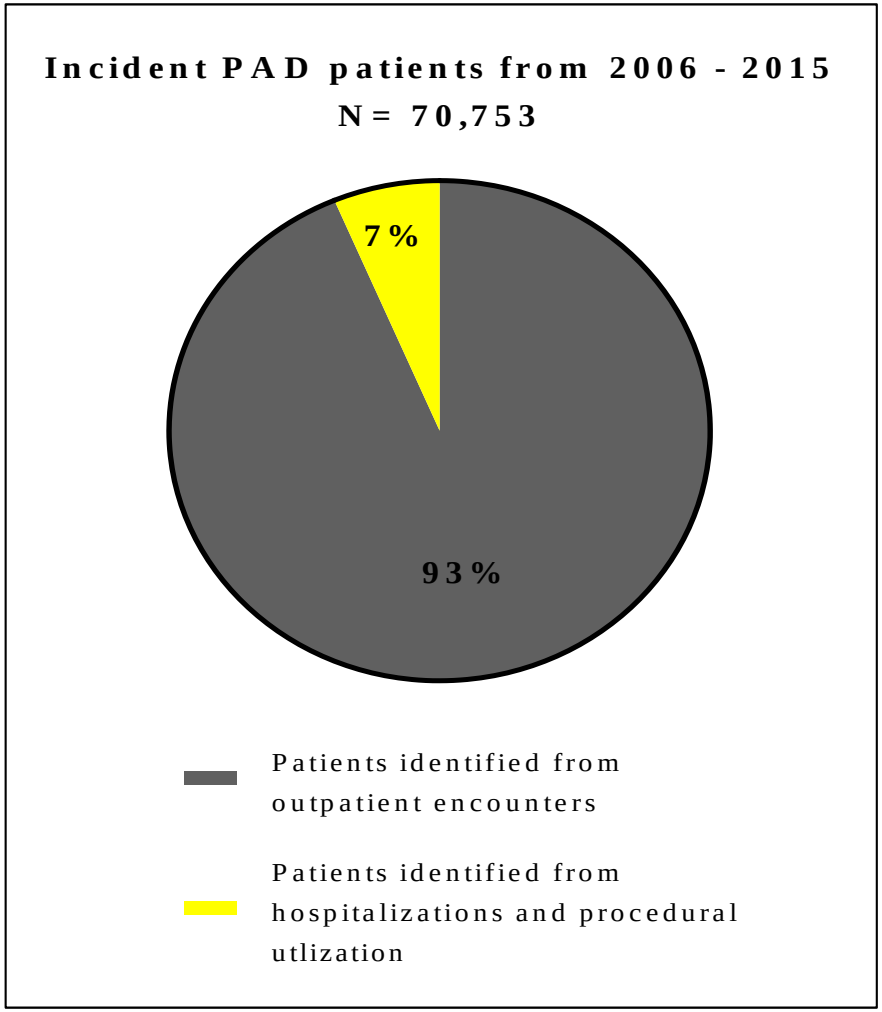
Supplementary Figure S2: Flow chart for identification of patients with incident peripheral artery disease: 2006-2015



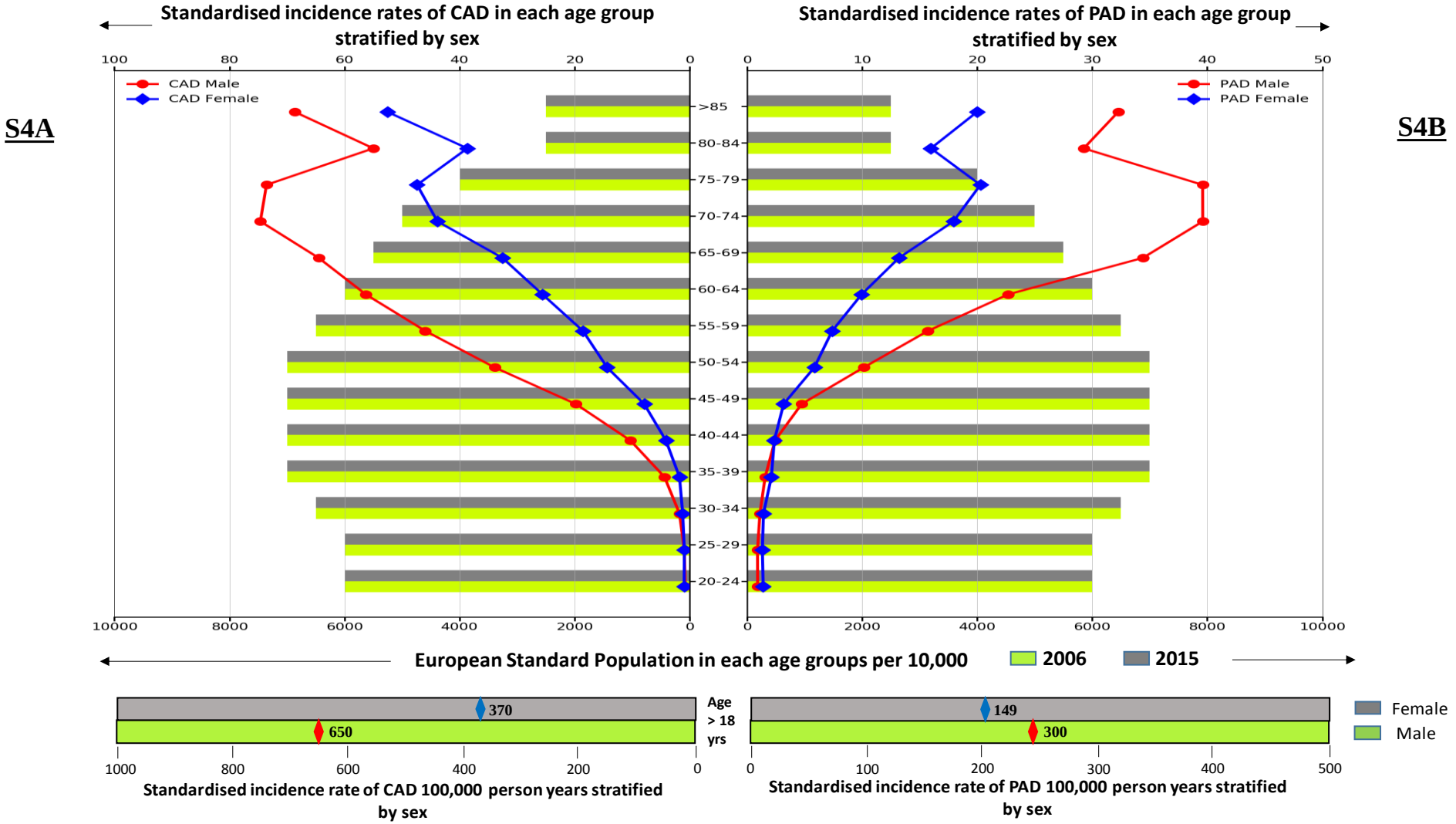
PAD: Peripheral artery disease; CAD: Coronary artery disease; CPRD: Clinical Practice Research Datalink; HES: Hospital Episode Statistics

Supplementary Figure S3: Percentage of incident CAD and incident PAD patients identified using primary care (Clinical Practice Research Datalink-Read codes) and hospital care records (Hospital Episode Statistics – ICD 10 and OPCS 4·6 for revascularization procedures)



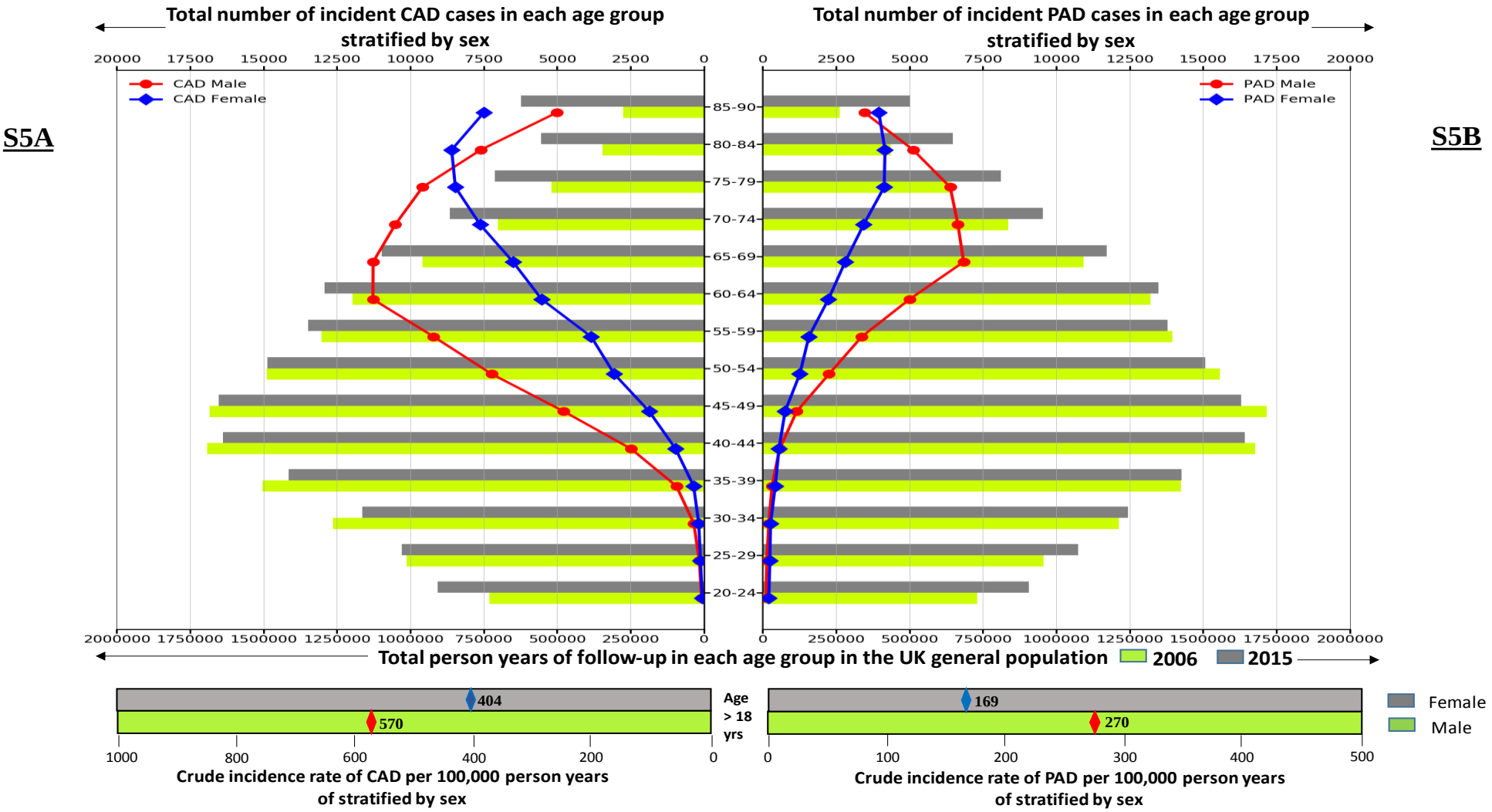


Supplementary Figure S4A: Standardised incidence of CAD in men and women; Figure S4B: Standardised incidence of PAD in men and women (from 2006 to 2015)



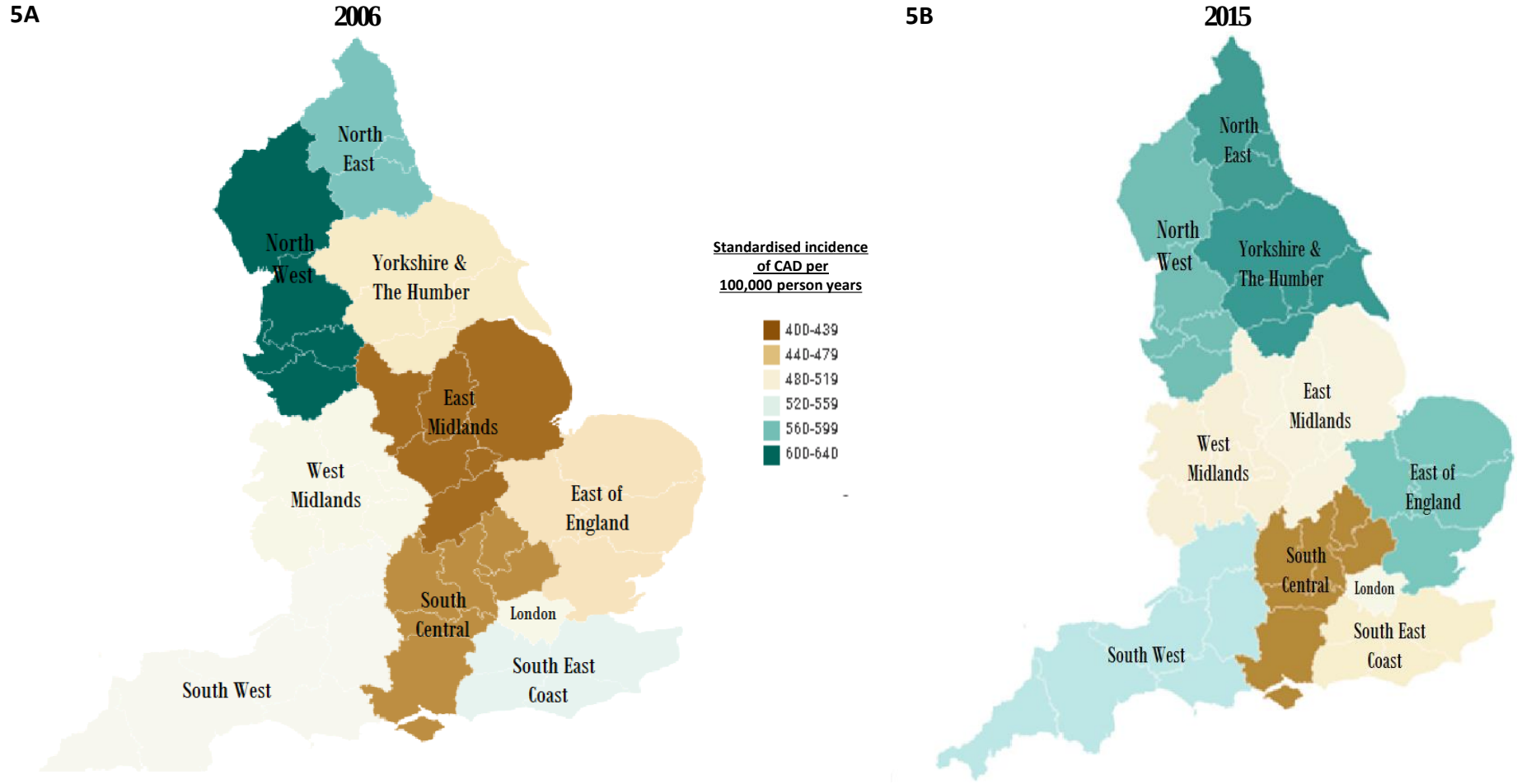
Age standardised incidence rates of CAD (S4A) and PAD (S4B) per 100,000 person years in from 2006 to 2015 in the UK.

Supplementary Figure S5A: Crude incidence of CAD in men and women; Figure S5B: Crude incidence of PAD in men and women (from 2006 to 2015)



Absolute number of cases of CAD (S5A) and PAD (S5B) in men and women within each age group per person years of follow up from 2006 to 2015 in the UK.

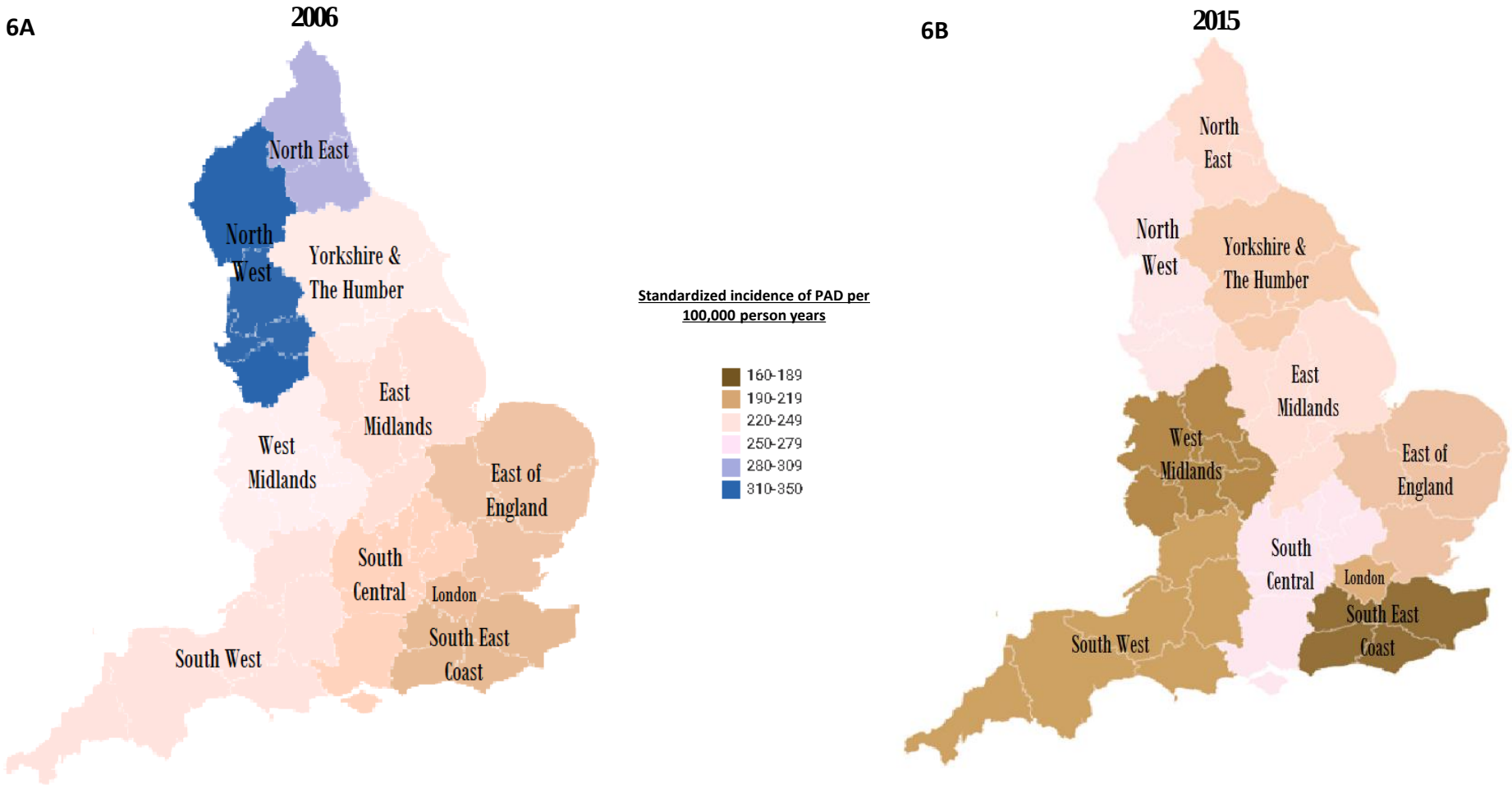
Supplementary Figure S6A and 6B; Regional variations in the standardised incidence of CAD in England 2006 vs 2015



***Incidence rates standardised for age and sex; Data on West Midlands for 5B is from 2013*

*** The decline in the standardised incidence of CAD between 2006 and 2015 was consistent across all regions, with much higher reductions in the northern regions.*

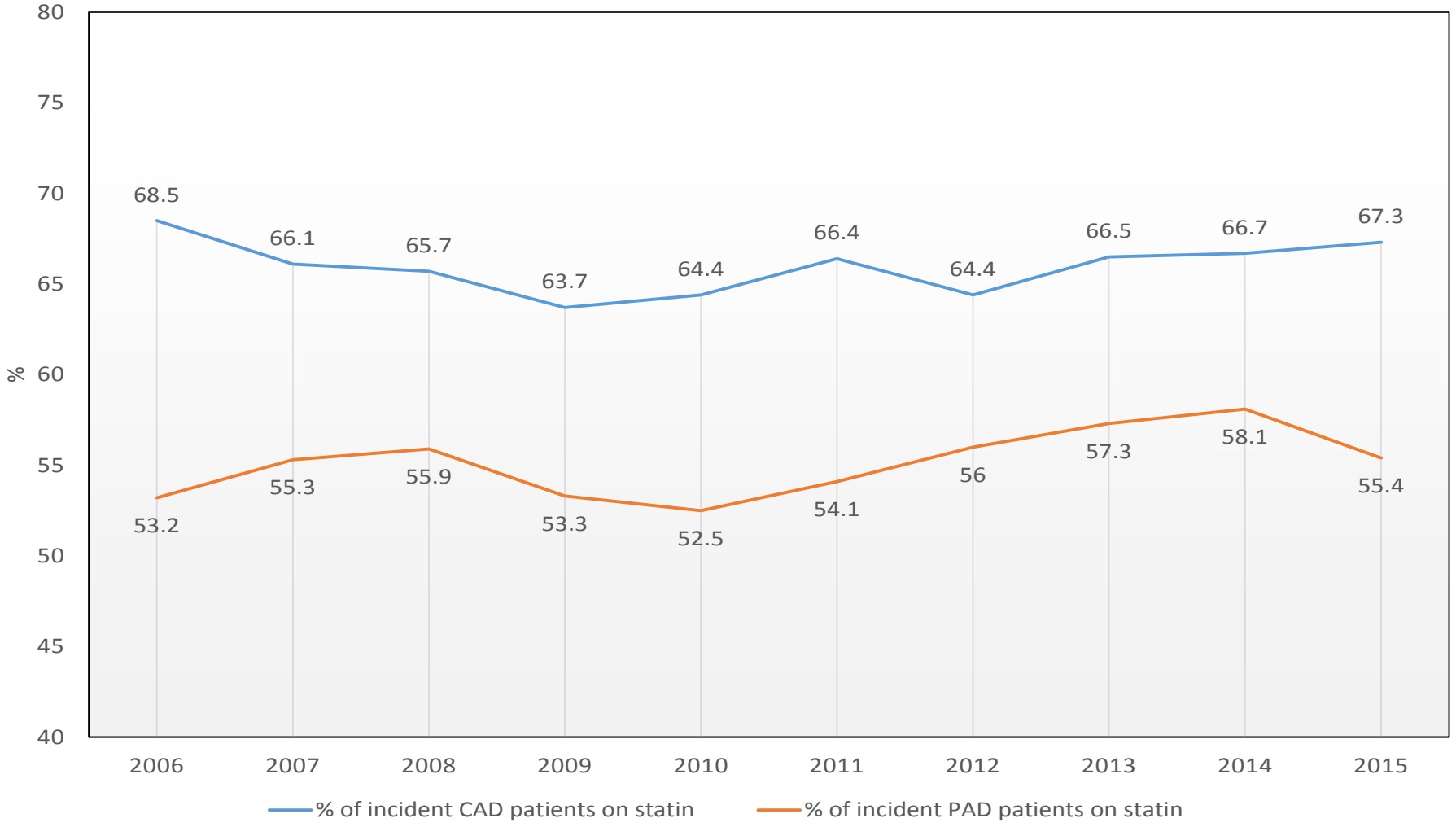
Supplementary Figure S7A and 7B; Regional variations in the standardised incidence of CAD in England 2006 vs 2015



***Incidence rates standardised for age and sex; Data on West Midlands for 6B is from 2013*

*** The decline in the standardised incidence of CAD between 2006 and 2015 was consistent across all regions, with much higher reductions in the northern regions.*

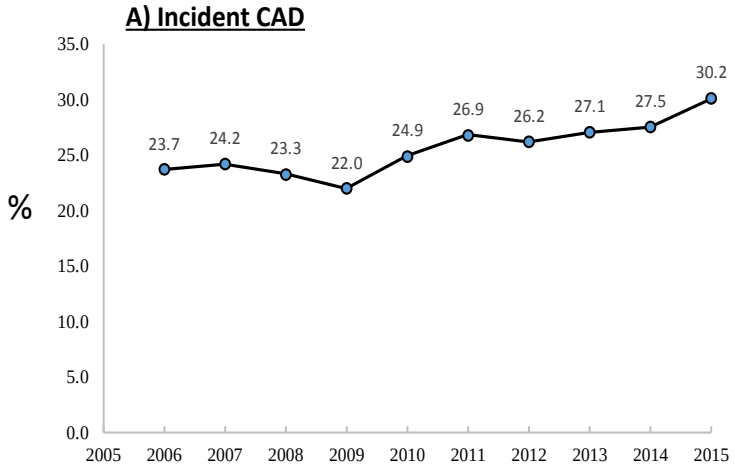
Supplementary Figure S8: Proportion of patients on long term statin therapy after an incident diagnosis of CAD and PAD from 2006 to 2015 in the UK

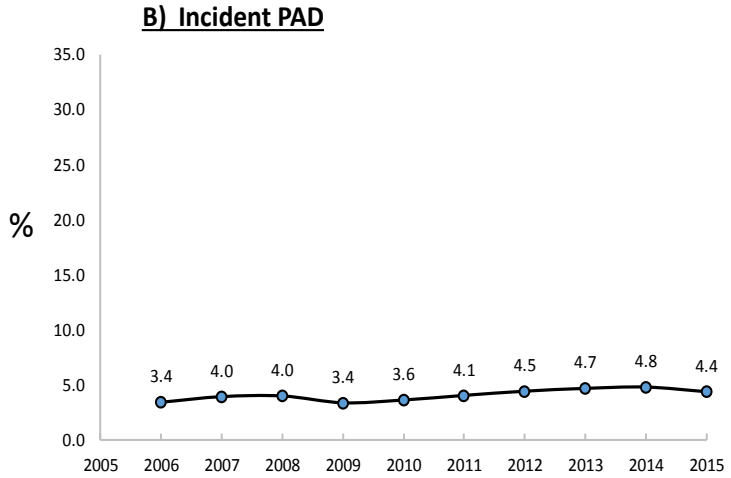


CAD: Coronary artery disease; PAD: Peripheral artery disease

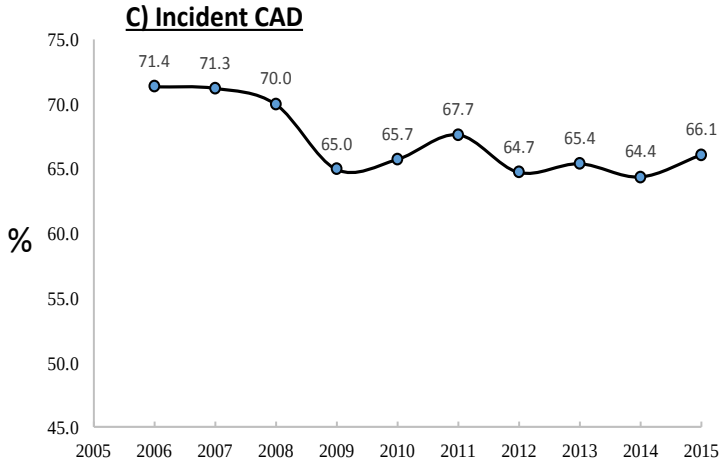
Supplementary Figure S9: Temporal trends in anti-platelet use among patients with incident CAD and PAD in the UK, 2006-2015

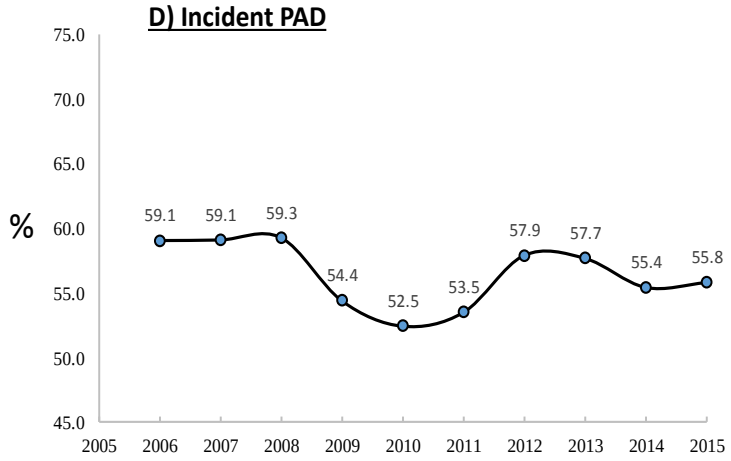
Proportion of CAD and PAD patients on dual anti-platelet therapy at 1 year after incident diagnosis





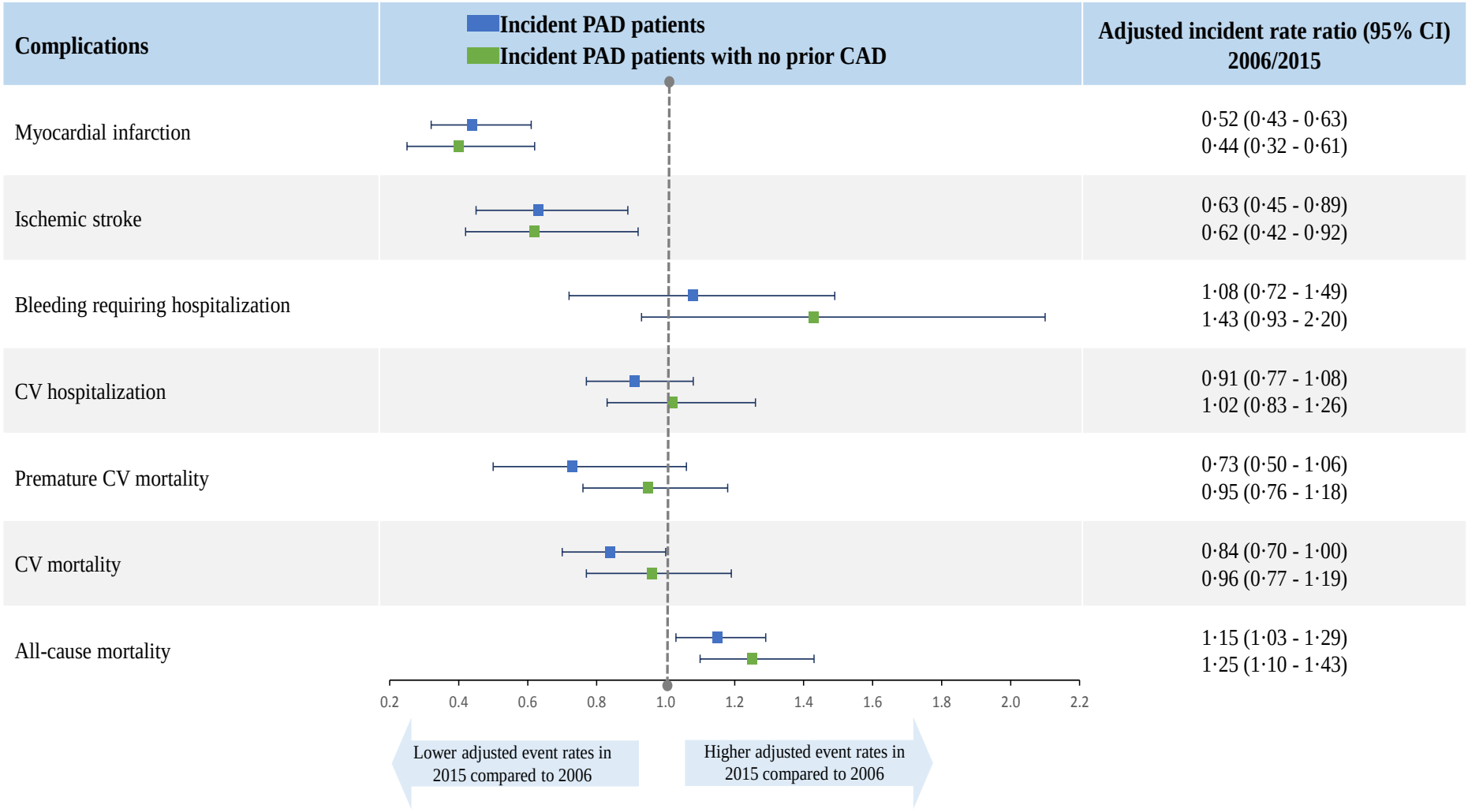
Proportion of CAD and PAD patients on at-least one anti-platelet therapy at 1 year after incident diagnosis





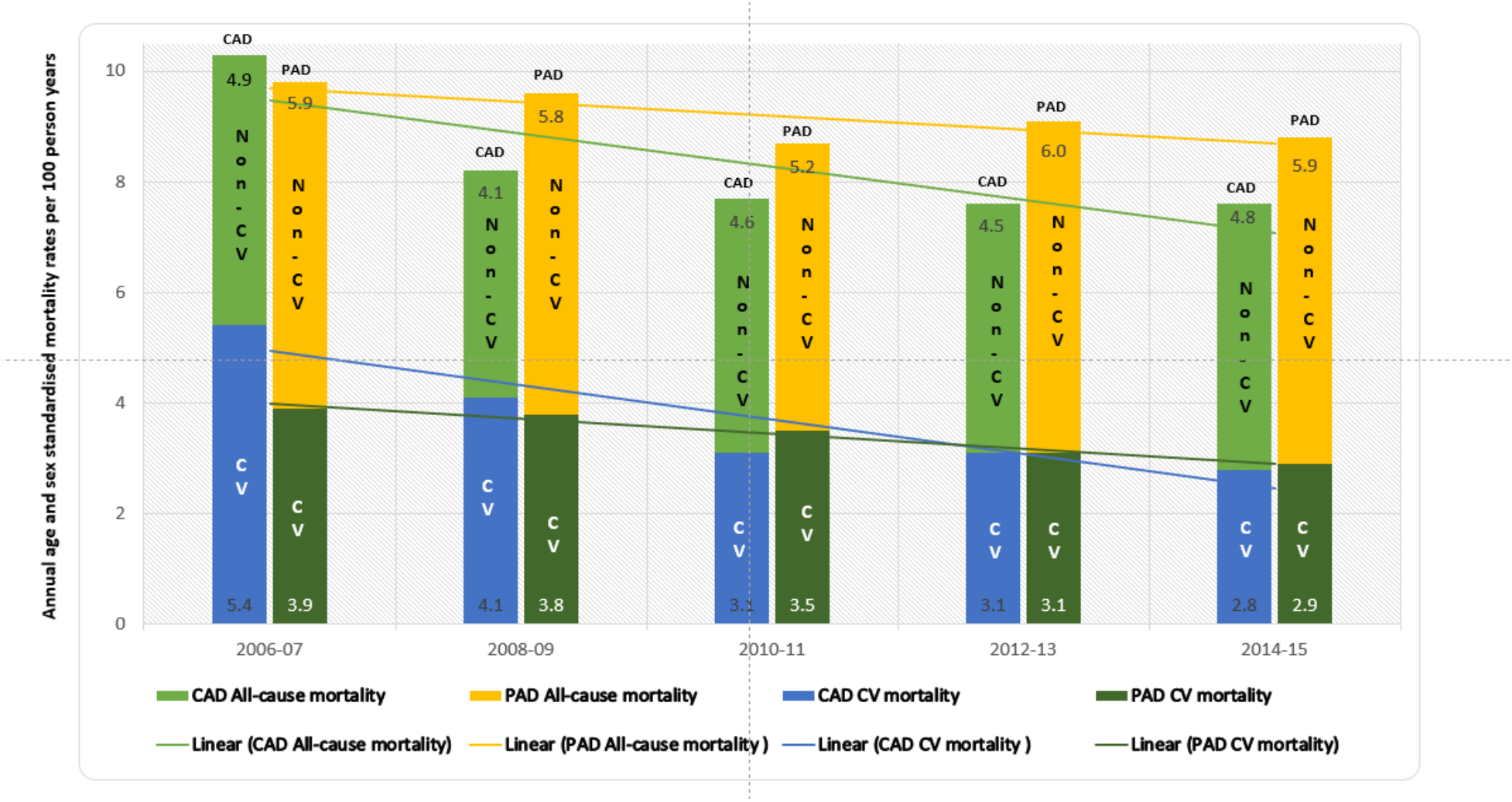
Significantly higher proportion of male patients were on dual antiplatelet therapy (men: 26.5% vs women: 17.3%) at 12 months for secondary prevention.

Supplementary Figure S10: Trends in the annual age and sex adjusted event rates of major vascular events, bleeding, hospitalisation and mortality among patients with incident PAD and incident PAD with no prior CAD in 2006 vs 2015



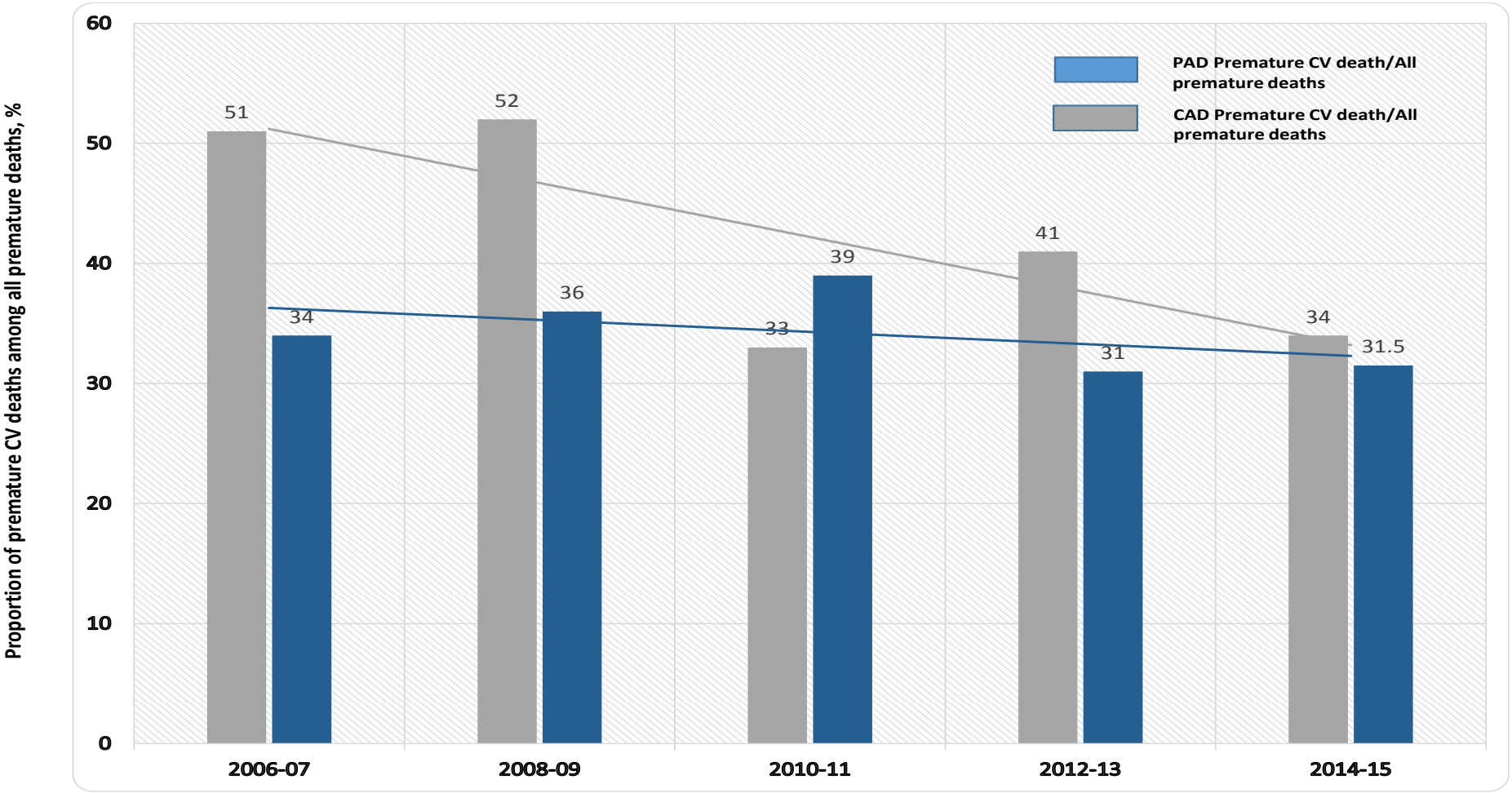
** *MI: Myocardial infarction, CV hospitalisation: cardiovascular hospitalisation (planned and unplanned), Premature CV death: Death <75 years of age due to cardiovascular cause, CV death: Death due to cardiovascular cause*

Supplementary Figure S11: Trends in annual standardised cardiovascular (CV) and all-cause mortality in patients with incident CAD and incident PAD from 2006 to 2015



CV:CV mortality, Non-CV: Non-CV mortality

Supplementary Figure S12: Proportion of premature all-cause mortality, defined as death < 75 years, attributable to premature cardiovascular deaths in patients with incident CAD and incident PAD from 2006 to 2015



This figure shows proportion of premature all-cause mortality, defined as death < 75 years, attributable to premature cardiovascular deaths

Supplementary Figure S13. Trends in the age and sex standardised incidence rates for MI, ischemic stroke and hospitalisation for bleeding from 2006 to 2015 in patients with incident CAD and incident PAD

Figure S11A; Incident CAD

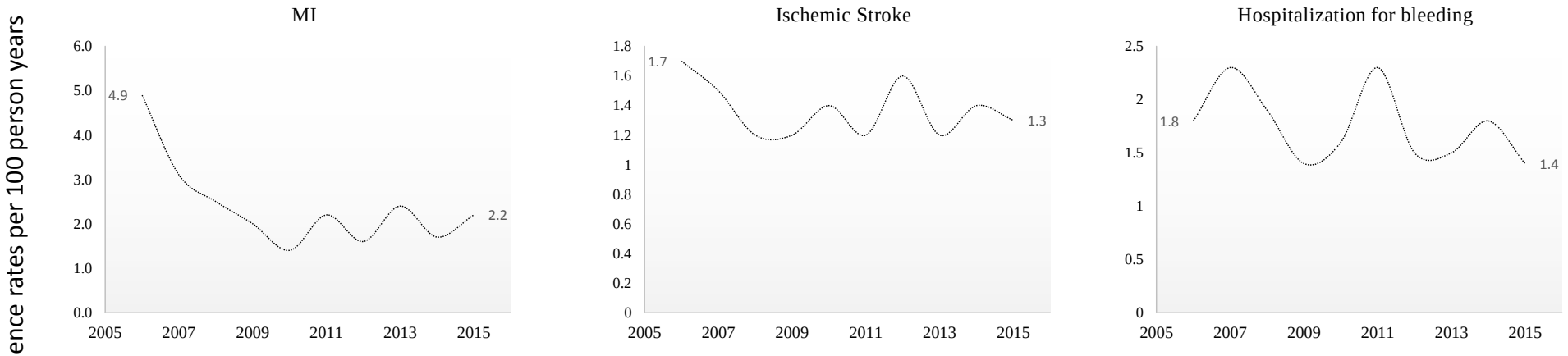
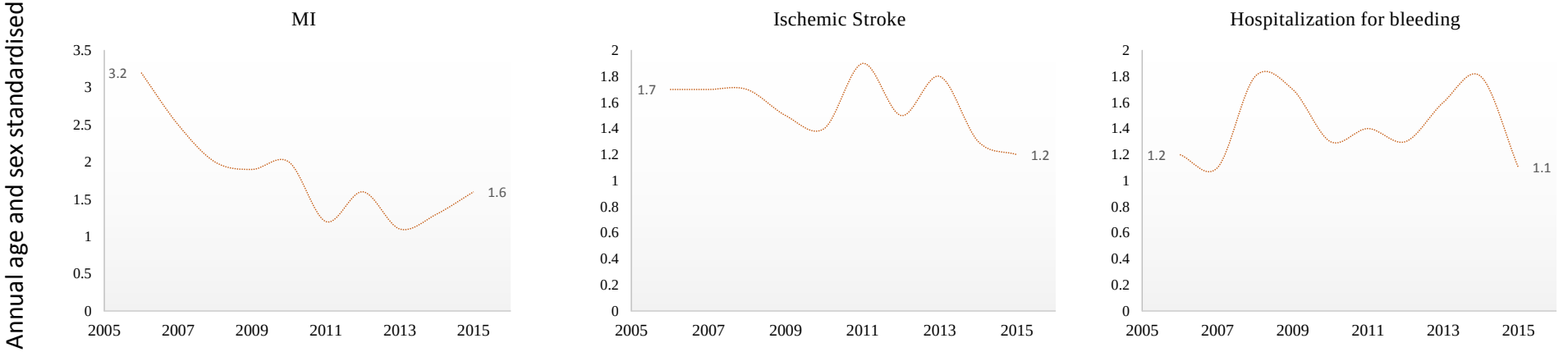


Figure S11B; Incident PAD



Supplementary Table S1. Crude and standardised incidence rates of acute myocardial infarction in 2006 and 2015

Age	Crude age specific incidence rates		Standardised incidence rates	
	2006	2015	2006	2015
20-24	2·30	2·06	0·14	0·12
25-29	4·40	0·96	0·26	0·06
30-34	4·70	7·80	0·31	0·51
35-39	14·60	24·00	1·02	1·68
40-44	36·70	39·90	2·57	2·79
45-49	67·00	86·60	4·69	6·06
50-54	109·34	137·80	7·65	9·65
55-59	147·40	177·25	9·58	11·52
60-64	195·40	220·50	11·72	13·23
65-69	260·10	241·03	14·31	13·26
70-74	323·40	272·60	16·17	13·63
75-79	424·30	364·70	16·97	14·59
80-84	520·52	434·30	13·01	10·86
>85	703·60	648·90	17·59	16·22
Cumulative rate/ 100,000 person years	**145·80**	**147·50**	**147·80**	**145·40**

Age and sex adjusted Incidence rate ratio; 0·99 (0·95 – 1·03)

Supplementary Table S2: Baseline characteristics of incident CAD and PAD patients included and excluded for statin analyses

	Incident CAD, 2006-2015		Incident PAD, 2006-2015	
	Included (n=121,101)	**Excluded (n=39,275)**	**Included (n=49,426)**	**Excluded (n=21,327)**
Age (years), mean (SD)	***68·0 (12·3)***	***72.7 (17.0)***	***70·6 (11.2)***	***70·0 (18.4)***
Sex				
Women	49,860 (37·3%)	18,311 (46.6%)	18,229 (36.9%)	9,861 (46.2%)
Men	70,734 (62·7%)	20,964 (53.4%)	31,196 (63.1%)	11,466 (53.8%)
Socioeconomic quintile				
Quintile 1	16,882 (20.7%)	6,128 (18.5%)	5,491 (18.3%)	2,950 (18.9%)
Quintile 2	18,650 (22.8%)	7,478 (22.6%)	6,666 (22.2%)	3,539 (22.6%)
Quintile 3	17,170 (21.0%)	7,003 (21.1%)	6,241 (20.8%)	3,350 (21.4%)
Quintile 4	15,802 (19.3%)	6,767 (20.4%)	6,436 (21.5%)	3,101 (19.8%)
Quintile 5 (most deprived)	13,134 (16.1%)	5,763 (17.4%)	5,118 (17.1%)	2,697 (17.3%)
Co-morbidities				
Diabetes Mellitus	22,352 (20·4%)	8,929 (21.0%)	12,686 (25·6%)	4,875 (22.9%)
Hypertension	73,537 (61·3%)	24,651 (62.8%)	33,321 (67.4%)	12,808 (60.1%)
Stroke	9,176 (7·8%)	4,103 (10.4%)	4,129 (8·4%)	2,224 (10.4%)
Peripheral arterial disease/Coronary artery disease	10,072 (6·8%)	3,065 (7.5%)	13,239 (26.8%)	4,732 (22.2%)
Chronic Kidney Disease	17, 188 (13·5%)	8,813 (22.4%)	9,220 (18.7%)	4,806 (22.5%)
COPD	10,353 (7·8%)	4,493 (11.4%)	6,200 (12·5%)	2,382 (11.2%)
Chronic Liver Disease	1,527(1·1%)	585 (1.5%)	731 (1·5%)	342 (1.6%)
Depression	9,825 (7·6%)	3,209 (8.2%)	3,870 (7·8%)	1,755 (8.2%)
Malignancy	9,245 (7·0%)	4,470 (11.4%)	4,432 (9.0%)	2,359 (11.1%)

COPD: Chronic obstructive pulmonary disease

** Prior history of PAD among patients with incident PAD and prior history of CAD among patients with incident PAD*

Supplementary Table S3: Proportion of patients with incidence CAD and PAD on statin, stratified by co-morbidities

	CAD (n=121,011)	PAD (n =49,426)
Total no of CAD/PAD patients on statins	80,169 (66·0%)	27,150 (54·9%)
Age in years		
40-49 years	5,590 (59·6%)	388 (31·8%)
50-59 years	15,170 (68·3%)	1,765 (50·1%)
60-69 years	33,274 (71·5%)	4,602 (58·9%)
70-79 years	32,549 (68·4%)	5,875 (61·1%)
> 80 years	12,827 (54·1%)	3,666 (47·1%)
Sex		
Women	29,681 (58·9%)	10,805 (57·4%)
Men	49,960 (70·1%)	5,491 (49·3%)
Ethnicity		
White	22,915 (66·8%)	5,168 (55·9%)
Non-white	19,088 (63·2%)	4,145 (53·4%)
Socioeconomic quintile		
Quintile 1	10,873 (64·4%)	3,001 (54·7%)
Quintile 2	11,776 (63·1%)	3,655 (54·5%)
Quintile 3	12,464 (60·9%)	3,315 (53·1%)
Quintile 4	9,670 (61·2%)	3,523 (54·7%)
Quintile 5	8,053 (61·2%)	2,796 (54·6%)
Smoking		
Current smoker	19,946 (66·6%)	8,265 (51·7%)
Co-morbidities		
Prior acute coronary syndrome	29,660 (82·9%)	4,906 (75·3%)
Diabetes Mellitus	16,276 (72·8%)	8,578 (67·6%)
Prior PAD/CAD	5,418 (70·0%)	9,641 (72·8%)
Stroke	6,179 (67·3%)	2,824 (68·4%)
Hypertension	48,789 (66·4%)	20,553 (61·7%)
Chronic Kidney Disease	10,768 (62·6%)	5,603 (60·7%)
Depression	6,071 (61·8%)	2,088 (54·0%)
COPD	6,223 (60·1%)	3,318 (53·5%)
Malignancy	5,610 (60·8%)	2,326 (52·5%)
Heart Failure	4,143 (54·8%)	2,229 (60·5%)
Dementia	2,296 (58·8%)	1,035 (56·2%)
Chronic Liver Disease	880 (57·6%)	348 (47·6%)

Supplementary Table S4: Complications of patients with incident PAD and no prior history of CAD (n= 34,283)

	Overall crude annual incidence rate	Overall age and sex standardised rates
MI	20·0 (18·1 - 21·6)	13·5 (12·4 - 14·7)
Ischemic Stroke	24·9 (23·1 - 26·8)	15·6 (14·3 - 16·9)
Bleeding	14·5 (13·3 - 15·7)	11·0 (10·1 - 12·0)
CV hospitalisation	85·3 (81·9 - 88·9)	57·0 (54·7 - 59·3)
CV mortality	68·4 (65·5 - 71·6)	32·6 (29·3 -36·0)
All-cause mortality	181·5 (176·6 - 186·5)	94·4 (91·8 - 97·0)

MI: Myocardial infarction, CV hospitalisation: cardiovascular hospitalisation (planned and unplanned), Premature CV death: Death <75 years of age due to cardiovascular cause, CV death: Death due to cardiovascular cause

Supplementary Table S5: Annual incident rates of amputation and acute limb ischemia among patients with incident PAD (from 2006 to 2015)

Outcomes	**Annual crude incidence rate/ 100 person years**	**Crude incidence rate ratio, 95% CI (2015 vs 2006)**	**Age and sex adjusted incidence rate ratio, 95% CI (2015 vs 2006)**
Amputation	2.2 (2·0 - 2.4)	1.2 (0.9 - 1.7)	1·2 (0.9 - 1·7)
Acute Limb ischemia	0.6 (0.5 - 0.7)	1.1 (0.3 - 3.3)	1.1 (0.4 - 3.0)

Annual crude incidence rates include annual incident rates of amputation and acute limb ischemia among all patients with incident PAD from 2006 to 2015 per 100 person years of follow up.

Crude incident rate ratio was calculated comparing annual crude incident rates of outcomes (amputations and acute limb ischemia) in 2015 vs 2006 (e.g., Crude incident rate ratio of 1.2 indicates a 20% increase in the rates of annual rates of amputation in 2015 when compared to incident PAD patients in 2006)

Age and sex adjusted incident rate ratio was calculated using Poisson regression model (comparing 2015 rates vs 2006 rates after adjusting for differences in age)

Supplementary Table S6: Clinical codes for identification of coronary artery disease (Read, ICD10 and OPCS 4.6)

Read codes (CPRD): Codes used for identification from GP encounters

Medcode	Readcode	Diagnosis
241	G30..00	Acute myocardial infarction
732	7928z00	Transluminal balloon angioplasty of coronary artery NOS
733	7A54000	Percutaneous transluminal angioplasty of artery NEC
737	792..11	Coronary artery bypass graft operations
1344	G340.12	Coronary artery disease
1430	G33..00	Angina pectoris
1431	G311.13	Unstable angina
1655	G340.11	Triple vessel disease of the heart
1676	G3z..00	Ischemic heart disease NOS
1677	G30..15	MI - acute myocardial infarction
1678	G308.00	Inferior myocardial infarction NOS
1792	G3...13	IHD - Ischemic heart disease
2901	7928.00	Transluminal balloon angioplasty of coronary artery
3159	792Dy00	Other specified other bypass of coronary artery
3704	G307.00	Acute sub endocardial infarction
3999	G340000	Single coronary vessel disease
4017	G32..00	Old myocardial infarction
5030	ZV45K00	[V]Presence of coronary artery bypass graft
5387	G301.00	Other specified anterior myocardial infarction
5413	G340.00	Coronary atherosclerosis
5674	ZV45K11	[V]Presence of coronary artery bypass graft - CABG
5703	7928.11	Percutaneous balloon coronary angioplasty
5744	7927500	Open angioplasty of coronary artery
5904	792..00	Coronary artery operations
6182	7929y00	Other therapeutic transluminal op on coronary artery OS
7134	7921.11	Other autograft bypass of coronary artery
7137	7920y00	Saphenous vein graft replacement of coronary artery OS
7320	G343.00	Ischemic cardiomyopathy
7347	G311100	Unstable angina
7442	7920200	Saphenous vein graft replacement of three coronary arteries
7609	7921z00	Other autograft replacement of coronary artery NOS
7634	7920100	Saphenous vein graft replacement of two coronary arteries
8312	7920.11	Saphenous vein graft bypass of coronary artery
8679	7920000	Saphenous vein graft replacement of one coronary artery
8935	G302.00	Acute inferolateral infarction
8942	7929400	Insertion of coronary artery stent
9276	G31y000	Acute coronary insufficiency
9413	G31y.00	Other acute and subacute ischemic heart disease
9414	7921.00	Other autograft replacement of coronary artery
9507	G307000	Acute non-Q wave infarction
9555	G33z500	Post infarct angina
10209	7921200	Autograft replacement of three coronary arteries NEC
10260	6A4..00	Coronary heart disease review
10562	G307100	Acute non-ST segment elevation myocardial infarction
10603	792z.00	Coronary artery operations NOS
11648	8B3k.00	Coronary heart disease medication review
11983	G311500	Acute coronary syndrome

Medcode	Readcode	Diagnosis
12139	G300.00	Acute anterolateral infarction
12229	G30X000	Acute ST segment elevation myocardial infarction
12734	SP07600	Coronary artery bypass graft occlusion
12804	G33z700	Stable angina
13185	662K.00	Angina control
13566	G30..11	Attack - heart
13571	G30..16	Thrombosis - coronary
14658	G30z.00	Acute myocardial infarction NOS
14782	662K200	Angina control - improving
14897	G301z00	Anterior myocardial infarction NOS
14898	G305.00	Lateral myocardial infarction NOS
15349	662Kz00	Angina control NOS
15373	662K100	Angina control - poor
15754	G34z.00	Other chronic ischemic heart disease NOS
16408	G32..11	Healed myocardial infarction
17464	G32..12	Personal history of myocardial infarction
17689	G30..17	Silent myocardial infarction
17872	G301100	Acute anteroseptal infarction
18118	G311400	Worsening angina
18135	6A2..00	Coronary heart disease annual review
18150	9Ob..00	Coronary heart disease monitoring administration
18249	7920.00	Saphenous vein graft replacement of coronary artery
18643	ZV45800	[V]Presence of coronary angioplasty implant and graft
18670	7928000	Percut transluminal balloon angioplasty one coronary artery
18842	G35..00	Subsequent myocardial infarction
18913	ZV45700	[V]Presence of aortocoronary bypass graft
19046	7929300	Rotary blade coronary angioplasty
19193	7923z00	Prosthetic replacement of coronary artery NOS
19402	7923.00	Prosthetic replacement of coronary artery
19413	7921100	Autograft replacement of two coronary arteries NEC
19542	662K000	Angina control - good
19655	G311.14	Angina at rest
19744	8I37.00	Coronary heart disease monitoring refused
20416	G3...12	Atherosclerotic heart disease
20903	7A6G100	Peroperative angioplasty
22020	792B000	Endarterectomy of coronary artery NEC
22383	G3y..00	Other specified ischemic heart disease
22647	7925311	LIMA single anastomosis
22828	7929000	Percutaneous transluminal laser coronary angioplasty
23078	G34y100	Chronic myocardial ischemia
23579	G310.00	Postmyocardial infarction syndrome
23892	G304.00	Posterior myocardial infarction NOS
24126	G360.00	Haemopericardium/current comp folow acut myocard infarct
24540	G34y000	Chronic coronary insufficiency
24783	G3...11	Arteriosclerotic heart disease
24888	7929.00	Other therapeutic transluminal operations on coronary artery
26863	G33z600	New onset angina
27951	G31..00	Other acute and subacute ischemic heart disease
27977	G31yz00	Other acute and subacute ischemic heart disease NOS
28138	G34..00	Other chronic ischemic heart disease
28554	G33zz00	Angina pectoris NOS

Medcode	Readcode	Diagnosis
28736	G30y000	Acute atrial infarction
28837	7925.11	Creation of bypass from mammary artery to coronary artery
29300	662K300	Angina control - worsening
29421	G344.00	Silent myocardial ischemia
29553	G366.00	Thrombosis atrium,auric append&vent/curr comp foll acute MI
29643	G303.00	Acute inferoposterior infarction
29758	G30X.00	Acute transmural myocardial infarction of unspecif site
30330	G309.00	Acute Q-wave infarct
30421	G30..13	Cardiac rupture following myocardial infarction (MI)
31519	7925100	Double implant of mammary arteries into coronary arteries
31540	7924200	Revision of bypass for three coronary arteries
31556	7922.00	Allograft replacement of coronary artery
31571	792y.00	Other specified operations on coronary artery
31679	7929z00	Other therapeutic transluminal op on coronary artery NOS
32272	G38..00	Postoperative myocardial infarction
32651	7922.11	Allograft bypass of coronary artery
32854	G30B.00	Acute posterolateral myocardial infarction
33461	7924.00	Revision of bypass for coronary artery
33471	792Dz00	Other bypass of coronary artery NOS
33620	792B.00	Repair of coronary artery NEC
33650	7929100	Percut transluminal coronary thrombolysis with streptokinase
33718	7925000	Double anastomosis of mammary arteries to coronary arteries
33735	7928100	Percut translum balloon angioplasty mult coronary arteries
34328	G311300	Refractory angina
34803	G30y.00	Other acute myocardial infarction
34963	792D.00	Other bypass of coronary artery
35277	9Ob1.00	Refuses coronary heart disease monitoring
35373	9Ob0.00	Attends coronary heart disease monitoring
35713	G34yz00	Other specified chronic ischemic heart disease NOS
36011	7923.11	Prosthetic bypass of coronary artery
36423	G36..00	Certain current complication follow acute myocardial infarct
36609	G342.00	Atherosclerotic cardiovascular disease
37657	G362.00	Ventric septal defect/curr comp fol acut myocardal infarctn
37682	7925.00	Connection of mammary artery to coronary artery
37719	7925y00	Connection of mammary artery to coronary artery OS
37908	9Ob6.00	Coronary heart disease monitoring verbal invitation
38609	G351.00	Subsequent myocardial infarction of inferior wall
38813	7A54500	Rotary blade angioplasty
39500	9Ob8.00	Coronary heart disease monitoring check done
39584	3889.00	Euroscore for angina
40429	G301000	Acute anteroapical infarction
40996	7929111	Percut translum coronary thrombolytic therapy- streptokinase
41221	G30y200	Acute septal infarction
41547	7928y00	Transluminal balloon angioplasty of coronary artery OS
41757	7927z00	Other open operation on coronary artery NOS
42304	7929500	Insertion of drug-eluting coronary artery stent
42462	7928200	Percut translum balloon angioplasty bypass graft coronary a
42708	7921300	Autograft replacement of four of more coronary arteries NEC
43939	793G.00	Perc translumin balloon angioplasty stenting coronary artery
44561	7921000	Autograft replacement of one coronary artery NEC
44585	792Bz00	Repair of coronary artery NOS

Medcode	Readcode	Diagnosis
44723	7925200	Single anast mammary art to left ant descend coronary art
45370	7922300	Allograft replacement of four or more coronary arteries
45809	G350.00	Subsequent myocardial infarction of anterior wall
45886	7922200	Allograft replacement of three coronary arteries
45960	8B27.00	Antianginal therapy
46017	G30yz00	Other acute myocardial infarction NOS
46112	G380.00	Postoperative transmural myocardial infarction anterior wall
46166	G35X.00	Subsequent myocardial infarction of unspecified site
46276	G381.00	Postoperative transmural myocardial infarction inferior wall
47637	Gyu3300	[X]Other forms of chronic ischemic heart disease
47788	7927.00	Other open operations on coronary artery
47798	9Ob2.00	Coronary heart disease monitoring default
48767	7922z00	Allograft replacement of coronary artery NOS
48822	7925011	LIMA sequential anastomosis
49735	G5y6.00	Rupture of papillary muscle
50372	14AH.00	H/O: Myocardial infarction in last year
51507	7925300	Single anastomosis of mammary artery to coronary artery NEC
51515	7920z00	Saphenous vein graft replacement coronary artery NOS
52517	Gyu3.00	[X]Ischemic heart diseases
52637	388E.00	Canadian Cardiovascular Society classification of angina
52938	7924000	Revision of bypass for one coronary artery
53546	P6y4z00	Coronary artery anomaly NOS
55092	792C000	Replacement of coronary arteries using multiple methods
55598	792C.00	Other replacement of coronary artery
55673	ZR3P.00	CLASP angina score
56990	7925z00	Connection of mammary artery to coronary artery NOS
57241	7922100	Allograft replacement of two coronary arteries
57634	7924z00	Revision of bypass for coronary artery NOS
59189	G363.00	Ruptur cardiac wall w'out haemopericard/cur comp fol ac MI
59350	ZR37.00	Canadian Cardiovascular Society classification of angina
59423	7922y00	Other specified allograft replacement of coronary artery
59940	G364.00	Ruptur chordae tendinae/curr comp fol acute myocard infarct
60067	793G000	Perc translum ball angio insert 1-2 drug elut stents cor art
60753	7926300	Single implantation thoracic artery into coronary artery NEC
61208	793Gz00	Perc translum balloon angioplasty stenting coronary art NOS
61310	7921y00	Other autograft replacement of coronary artery OS
61670	889A.00	Diab mellit insulin-glucose infus acute myocardial infarct
62608	7926000	Double anastom thoracic arteries to coronary arteries NEC
62626	G30y100	Acute papillary muscle infarction
63153	7924500	Revision of implantation of thoracic artery into heart
63467	G306.00	True posterior myocardial infarction
66236	7923200	Prosthetic replacement of three coronary arteries
66583	7929200	Percut translum inject therap subst to coronary artery NEC
66664	7923100	Prosthetic replacement of two coronary arteries
67554	7924100	Revision of bypass for two coronary arteries
67591	7926200	Single anastomosis of thoracic artery to coronary artery NEC
67761	7923300	Prosthetic replacement of four or more coronary arteries
68123	7925312	RIMA single anastomosis
68139	7925400	Single implantation of mammary artery into coronary artery
68401	Gyu3200	[X]Other forms of acute ischemic heart disease
68748	G38z.00	Postoperative myocardial infarction, unspecified

Medcode	Readcode	Diagnosis
69247	792By00	Other specified repair of coronary artery
69474	G365.00	Rupture papillary muscle/curr comp fol acute myocard infarct
69776	SP00300	Mechanical complication of coronary bypass
70111	7922000	Allograft replacement of one coronary artery
70160	9Ob9.00	Coronary heart disease monitoring telephone invite
70185	7A54800	Percutaneous transluminal atherectomy
70755	792Cz00	Replacement of coronary artery NOS
72562	G353.00	Subsequent myocardial infarction of other sites
72780	7926z00	Connection of other thoracic artery to coronary artery NOS
85947	793G200	Perc translum balloon angioplasty insert 1-2 stents cor art
86071	7928300	Percut translum cutting balloon angioplasty coronary artery
86773	7A56400	Percutaneous transluminal balloon angioplasty of artery
87849	793G100	Perc tran ball angio ins 3 or more drug elut stents cor art
92233	7925012	RIMA sequential anastomosis
92267	G5yy200	Papillary muscle dysfunction
92419	7923000	Prosthetic replacement of one coronary artery
92927	793G300	Percutaneous cor balloon angiop 3 more stents cor art NEC
93618	7929600	Percutaneous transluminal atherectomy of coronary artery
93828	792Cy00	Other specified replacement of coronary artery
95382	7927y00	Other specified other open operation on coronary artery
95550	8H2V.00	Admit ischemic heart disease emergency
96537	793Gy00	OS perc translumina balloon angioplast stenting coronary art
96804	7926.00	Connection of other thoracic artery to coronary artery
96838	Gyu3400	[X]Acute transmural myocardial infarction of unspecif site
97953	7924y00	Other specified revision of bypass for coronary artery
98295	ZRB1.00	Euroscore for angina
99991	Gyu3600	[X]Subsequent myocardial infarction of unspecified site
100437	9hM..00	Exception reporting: myocardial infarction quality indicator
100496	8CEJ.00	Coronary heart disease leaflet given
101121	8L40.00	Coronary artery bypass graft operation planned
101569	7924300	Revision of bypass for four or more coronary arteries
103655	187..00	Frequency of angina
103932	8CMP.00	Coronary heart disease care plan
105184	792E.00	Percutaneous coronary intervention
106812	G383.00	Postoperative transmural myocardial infarction unspec site
107406	792E000	Emergency percutaneous coronary intervention
107967	661M000	Angina self-management plan agreed
109035	Gyu3500	[X]Subsequent myocardial infarction of other sites
109391	661N000	Angina self-management plan review

ICD-10 codes (HES): Codes used for identification of CAD from hospital admissions

ICD10 codes	Diagnosis
I20	Angina pectoris
I21	Acute myocardial infarction
I22	Subsequent myocardial infarction
I23	Certain current complications following acute myocardial infarction
I24	Other acute ischemic heart diseases
I25	Chronic ischemic heart disease

OPCS 4.6 codes (HES): Codes used for identification of CAD from revascularization procedures

OPCS 4.6	Procedure
K49.1	Percutaneous transluminal balloon angioplasty of one coronary artery
K49.2	Percutaneous transluminal balloon angioplasty of multiple coronary arteries
K49.3	Percutaneous transluminal balloon angioplasty of bypass graft of coronary artery
K49.4	Percutaneous transluminal cutting balloon angioplasty of coronary artery
K49.8	Other specified transluminal balloon angioplasty of coronary artery
K49.9	Unspecified transluminal balloon angioplasty of coronary artery
K50.1	Percutaneous transluminal laser coronary angioplasty
K50.2	Percutaneous transluminal coronary thrombolysis using streptokinase
K50.3	Percutaneous transluminal injection of therapeutic substance into coronary artery NEC
K50.4	Percutaneous transluminal atherectomy of coronary artery
K50.8	Other specified other therapeutic transluminal operations on coronary artery
K50.9	Unspecified other therapeutic transluminal operations on coronary artery
K75.1	Percutaneous transluminal balloon angioplasty and insertion of 1-2 drug-eluting stents into coronary artery
K75.2	Percutaneous transluminal balloon angioplasty and insertion of 3 or more drug-eluting stents into coronary artery
K75.3	Percutaneous transluminal balloon angioplasty and insertion of 1-2 stents into coronary artery
K75.4	Percutaneous transluminal balloon angioplasty and insertion of 3 or more stents into coronary artery NEC
K75.8	Other specified percutaneous transluminal balloon angioplasty and insertion of stent into coronary artery
K75.9	Unspecified percutaneous transluminal balloon angioplasty and insertion of stent into coronary artery
K40.1	Saphenous vein graft replacement of one coronary artery
K40.2	Saphenous vein graft replacement of two coronary arteries
K40.3	Saphenous vein graft replacement of three coronary arteries
K40.4	Saphenous vein graft replacement of four or more coronary arteries
K40.8	Other specified saphenous vein graft replacement of coronary artery
K40.9	Unspecified saphenous vein graft replacement of coronary artery
K41.1	Autograft replacement of one coronary artery NEC
K41.2	Autograft replacement of two coronary arteries NEC
K41.3	Autograft replacement of three coronary arteries NEC
K41.4	Autograft replacement of four or more coronary arteries NEC
K41.8	Other specified other autograft replacement of coronary artery
K41.9	Unspecified other autograft replacement of coronary artery
K42.1	Allograft replacement of one coronary artery
K42.2	Allograft replacement of two coronary arteries

OPCS 4.6	Procedure
K42.3	Allograft replacement of three coronary arteries
K42.4	Allograft replacement of four or more coronary arteries
K42.8	Other specified allograft replacement of coronary artery
K42.9	Unspecified allograft replacement of coronary artery
K43.1	Prosthetic replacement of one coronary artery
K43.2	Prosthetic replacement of two coronary arteries
K43.3	Prosthetic replacement of three coronary arteries
K43.4	Prosthetic replacement of four or more coronary arteries
K43.8	Other specified prosthetic replacement of coronary artery
K43.9	Unspecified prosthetic replacement of coronary artery
K44.1	Replacement of coronary arteries using multiple methods
K44.2	Revision of replacement of coronary artery
K44.8	Other specified other replacement of coronary artery
K44.9	Unspecified other replacement of coronary artery
K45.1	Double anastomosis of mammary arteries to coronary arteries
K45.2	Double anastomosis of thoracic arteries to coronary arteries NEC
K45.3	Anastomosis of mammary artery to left anterior descending coronary artery
K45.4	Anastomosis of mammary artery to coronary artery NEC
K45.5	Anastomosis of thoracic artery to coronary artery NEC
K45.6	Revision of connection of thoracic artery to coronary artery
K45.8	Other specified connection of thoracic artery to coronary artery
K45.9	Unspecified connection of thoracic artery to coronary artery
K46.1	Double implantation of mammary arteries into heart
K46.2	Double implantation of thoracic arteries into heart NEC
K46.3	Implantation of mammary artery into heart NEC
K46.4	Implantation of thoracic artery into heart NEC
K46.5	Revision of implantation of thoracic artery into heart
K46.8	Other specified other bypass of coronary artery
K46.9	Unspecified other bypass of coronary artery
K47.1	Endarterectomy of coronary artery

Supplementary Table S7. Clinical codes for identification of peripheral artery disease (Read, ICD10 and OPCS 4.6 codes)

Read codes (CPRD): Codes used for identification from GP encounter

Readcode	Medcode	Diagnosis
14AE.00	16993	H/O: aortic aneurysm
14NB.00	59534	H/O: Peripheral vascular disease procedure
16I..00	7975	Claudication distance
2G63.00	9561	Ischemic toe
38DJ.00	98556	Edinburgh claudication questionnaire
585I000	104467	Abdominal aortic aneurysm screen ultrasound scan abnormal
5C10.00	12413	Carotid artery doppler abnormal
662U.00	18499	Peripheral vascular disease monitoring
66f3.00	103613	Aortic aneurysm monitoring
68B5100	101698	Aortic aneurysm screening abnormal
7A10100	23352	Bypass aorta by anastomosis axillary to femoral artery NEC
7A11.00	52358	Replacement of aneurysmal bifurcation of aorta
7A11000	96654	Emerg repl aneurysm bifurc aorta by anast aorta to fem art
7A11200	69922	Emerg repl aneurysm bifurc aorta by anast aorta to iliac a
7A11211	92925	Y graft of abdominal Aortic aneurysm (emergency)
7A11300	56510	Replace aneurysm bifurc aorta by anast aorta to iliac artery
7A11311	51166	Y graft abdominal Aortic aneurysm
7A11y00	62301	Replacement of aneurysmal bifurcation of aorta OS
7A11z00	66761	Replacement of aneurysmal bifurcation of aorta NOS
7A12000	48755	Emerg bypass bifurc aorta by anast aorta to femoral artery
7A12100	2761	Bypass bifurc aorta by anastom aorta to femoral artery NEC
7A12300	15532	Bypass bifurcation aorta by anastom aorta to iliac artery
7A13.11	17220	Emergency repair of aortic aneurysm
7A13100	93060	Emerg replace aneurysm thor aorta by anastom aorta to aorta
7A13300	66232	Emerg replace aneurysm infrarenal aorta by anast aorta/aorta
7A13400	54192	Emerg replace aneurysm abdom aorta by anast aorta/aorta NEC
7A13411	63408	Tube graft abdominal Aortic aneurysm (emergency)
7A14.11	1736	Aortic aneurysm repair
7A14100	42444	Replace aneurysm thoracic aorta by anast of aorta/aorta NEC
7A14400	19996	Replace aneurysm abdominal aorta by anast aorta to aorta NEC
7A14411	26232	Tube graft of Abdominal aortic aneurysm
7A1B000	70446	Endovascular stenting infrarenal abdominal aortic aneurysm
7A1B000	70446	Endovascular stenting infrarenal abdominal aortic aneurysm
7A1B200	51061	Endovascular stenting of thoracic aortic aneurysm
7A1B300	83527	Endovascular stenting of aortic dissection in any position
7A1B800	97217	Endovascul insert stent infrarenal abdominal aortic aneurysm
7A1B900	106780	Endovascular insertion stent for suprarenal aortic aneurysm
7A1BA00	98542	Endovascular insertion of stent for thoracic aortic aneurysm
7A1BB00	99787	Endovascular ins stent for aortic dissection in any position
7A1BC00	99859	Endovas insert stent for aortic aneurysm of bifurcation NEC
7A1C000	83577	Endovas ins stent graft for infrarenal abdom aortic aneurysm
7A1C100	94682	Endovas insert of stent graft for suprarenal aortic aneurysm
7A1C300	89714	Endov ins stent graft for aortic dissection in any position
7A20000	15007	Replacement of carotid artery using graft
7A20200	20811	Bypass to carotid artery NEC
7A20400	2654	Endarterectomy of carotid artery NEC

Readcode	Medcode	Diagnosis
7A21000	73022	Repair of carotid artery NEC
7A21z00	70235	Other open operation on carotid artery NOS
7A22000	29973	Percutaneous transluminal angioplasty of carotid artery
7A22z00	41703	Transluminal operation on carotid artery NOS
7A27C00	45308	Operation on aneurysm of subclavian artery
7A28000	31723	Percutaneous transluminal angioplasty of subclavian artery
7A28100	37465	Percutaneous transluminal angioplasty of brachial artery
7A28200	55074	Percutaneous transluminal angioplasty of vertebral artery
7A32000	25844	Percutaneous transluminal angioplasty of renal artery
7A34D00	91084	Operation on aneurysm of superior mesenteric artery NEC
7A34E00	61042	Operation on aneurysm of inferior mesenteric artery NEC
7A34K00	66633	Operation on aneurysm visceral branch of abdominal aorta NEC
7A35000	46164	Percutaneous transluminal angioplasty of coeliac artery NEC
7A35300	41220	Percutaneous transluminal angioplasty suprarenal artery NEC
7A40.00	59756	Replacement of aneurysmal iliac artery
7A40.11	103347	Replacement of aneurysmal iliac artery by anastomosis
7A40000	96699	Emerg replace aneurysm iliac art by iliac/femoral art anast
7A40200	109431	Emerg replace aneurysmal iliac artery by fem/fem art anast
7A40A00	99727	Replace aneurysm iliac art by aorta/ext iliac art anast NEC
7A40y00	106488	Other specified replacement of aneurysmal iliac artery
7A40z00	95503	Replacement of aneurysmal iliac artery NOS
7A41.00	21927	Other bypass of iliac artery
7A41.11	101910	Other bypass of iliac artery by anastomosis
7A41100	28616	Bypass iliac artery by iliac/femoral artery anastomosis NEC
7A41200	72448	Emerg bypass iliac artery by femoral/femoral art anast NEC
7A41300	36443	Bypass iliac artery by femoral/femoral art anastomosis NEC
7A41900	32492	Bypass common iliac artery by aorta/com iliac art anast NEC
7A41D00	100036	Bypass iliac artery by iliac/iliac artery anastomosis NEC
7A41z00	38921	Other bypass of iliac artery NOS
7A43200	39749	Operation on aneurysm of iliac artery NEC
7A44000	10827	Percutaneous transluminal angioplasty of iliac artery
7A45.00	61666	Emergency replacement of aneurysmal femoral/popliteal artery
7A45.12	103988	Emergency replacement of aneurysmal common femoral artery
7A45.14	46125	Emergency replacement of aneurysmal popliteal artery
7A45.15	94784	Emergency replacement aneurysmal superficial femoral artery
7A45000	55476	Emerg replace aneurysm fem art by fem/pop art anast c prosth
7A45200	62025	Emerg replace aneurysm fem art by fem/pop anast c vein graft
7A45700	89470	Emerg replace aneurysm pop art by pop/tib anast c vein graft
7A45C00	110617	Emerg replace aneurysm fem artery by fem/fem art anastomosis
7A45D00	55394	Emerg replace aneurysm pop artery by pop/fem art anastomosis
7A45y00	103044	Emergency replacement aneurysmal femoral/popliteal artery OS
7A46.00	69346	Other replacement of aneurysmal femoral artery
7A46.11	68385	Other replacement aneurysmal femoral artery by anastomosis
7A46.14	44439	Other replacement of aneurysmal popliteal artery
7A46.15	103731	Other replacement of aneurysmal superficial femoral artery
7A46000	96472	Replace aneurysm fem art by fem/pop art anastom c prosth NEC
7A46100	58092	Replace aneurysm pop art by pop/pop art anastom c prosth NEC
7A46300	71141	Replace aneurysm pop art by pop/pop a anast c vein graft NEC
7A46C00	97661	Replace aneurysm fem artery by fem/fem art anastomosis NEC
7A46D00	95416	Replace aneurysm popliteal artery by pop/fem anastomosis NEC
7A46y00	94556	Other replacement of aneurysmal femoral/popliteal artery OS

Readcode	Medcode	Diagnosis
7A46z00	96656	Other replacement of aneurysmal femoral/popliteal artery NOS
7A47.00	9099	Other emergency bypass of femoral artery or popliteal artery
7A47.12	100113	Other emergency bypass of common femoral artery
7A47.13	63238	Other emergency bypass of deep femoral artery
7A47.15	97606	Other emergency bypass of superficial femoral artery
7A47.16	11766	Other emergency bypass of femoral artery
7A47C00	48939	Emerg bypass femoral artery by fem/fem art anastomosis NEC
7A48.12	37787	Other bypass of common femoral artery
7A48000	27580	Bypass femoral artery by fem/pop art anast c prosthesis NEC
7A48200	28030	Bypass femoral artery by fem/pop art anast c vein graft NEC
7A48400	39877	Bypass femoral artery by fem/tib art anast c prosthesis NEC
7A48600	41823	Bypass femoral artery by fem/tib art anast c vein graft NEC
7A48800	67982	Bypass femoral artery by fem/peron a anast c prosthesis NEC
7A48A00	53675	Bypass femoral artery by fem/peron a anast c vein graft NEC
7A48C00	45428	Bypass femoral artery by femoral/femoral art anastomosis NEC
7A48y00	42640	Other bypass of femoral artery or popliteal artery OS
7A4A400	51124	Ligation of aneurysm of popliteal artery
7A4A500	28840	Operation on aneurysm of femoral artery NEC
7A4B000	6356	Percutaneous transluminal angioplasty of femoral artery
7A4B100	29112	Percutaneous transluminal angioplasty of popliteal artery
9N4h.00	43001	DNA - Did not attend peripheral vascular disease clinic
9m1..00	106224	Peripheral vascular disease monitoring invitation
9m10.00	106260	Peripheral vascular disease monitoring first letter
9m11.00	106660	Peripheral vascular disease monitoring second letter
9m12.00	106855	Peripheral vascular disease monitoring third letter
C107.00	35399	Diabetes mellitus with peripheral circulatory disorder
C107000	70448	Diabetes mellitus, juvenile +peripheral circulatory disorder
C107100	63357	Diabetes mellitus, adult, + peripheral circulatory disorder
C107200	33807	Diabetes mellitus, adult with gangrene
C107300	69124	IDDM with peripheral circulatory disorder
C107400	56803	NIDDM with peripheral circulatory disorder
C107z00	65025	Diabetes mellitus NOS with peripheral circulatory disorder
C109F00	54212	Non-insulin-dependent d m with peripheral angiopath
C109F11	54899	Type II diabetes mellitus with peripheral angiopathy
C109F12	60699	Type 2 diabetes mellitus with peripheral angiopathy
C10EG00	93468	Type 1 diabetes mellitus with peripheral angiopathy
C10F500	12736	Type 2 diabetes mellitus with gangrene
C10F511	104323	Type II diabetes mellitus with gangrene
C10FF00	37806	Type 2 diabetes mellitus with peripheral angiopathy
C10FF11	104639	Type II diabetes mellitus with peripheral angiopathy
G631.00	4240	Carotid artery occlusion
G634.00	2652	Carotid artery stenosis
G673000	22018	Dissection of cerebral arteries, nonruptured
G673200	12634	Carotid artery dissection
G673300	97122	Vertebral artery dissection
G700.00	1318	Aortic atherosclerosis
G700.11	19155	Aorto-iliac disease
G701.00	16284	Renal artery atherosclerosis
G701011	107071	ARAS - Atherosclerotic renal artery stenosis
G702.00	14797	Extremity artery atheroma
G702z00	16260	Extremity artery atheroma NOS

Readcode	Medcode	Diagnosis
G703.00	12888	Acquired renal artery stenosis
G70y000	37199	Carotid artery atherosclerosis
G70y011	22677	Carotid artery disease
G71..00	1735	Aortic aneurysm
G710.00	16521	Dissecting aortic aneurysm
G711.00	27563	Thoracic aortic aneurysm which has ruptured
G711.11	16800	Ruptured thoracic aortic aneurysm
G712.00	23532	Thoracic aortic aneurysm without mention of rupture
G713.00	17767	Abdominal aortic aneurysm which has ruptured
G713.11	13572	Ruptured abdominal aortic aneurysm
G713000	63920	Ruptured suprarenal aortic aneurysm
G714.00	1867	Abdominal aortic aneurysm without mention of rupture
G714.00	1867	Abdominal aortic aneurysm without mention of rupture
G714.11	17345	AAA - Abdominal aortic aneurysm without mention of rupture
G714100	28109	Inflammatory abdominal aortic aneurysm
G714200	101379	Infrarenal abdominal aortic aneurysm
G715.00	15304	Ruptured aortic aneurysm NOS
G715000	11430	Thoracoabdominal aortic aneurysm, ruptured
G715000	11430	Thoracoabdominal aortic aneurysm, ruptured
G716.00	16034	Aortic aneurysm without mention of rupture NOS
G716000	40787	Thoracoabdominal aortic aneurysm, without mention of rupture
G71z.00	6872	Aortic aneurysm NOS
G720.00	59492	Aneurysm of artery of arm
G722000	16395	Aneurysm of common iliac artery
G722100	60879	Aneurysm of external iliac artery
G722200	58794	Aneurysm of internal iliac artery
G722z00	59671	Aneurysm of iliac artery NOS
G723.00	45000	Aneurysm of leg artery
G723000	6684	Aneurysm of femoral artery
G723100	16366	Aneurysm of popliteal artery
G723200	67026	Aneurysm of anterior tibial artery
G723300	69847	Aneurysm of dorsalis pedis artery
G723400	72062	Aneurysm of posterior tibial artery
G723500	31055	Ruptured popliteal artery aneurysm
G723600	40524	Post radiological femoral false aneurysm
G725.00	110372	Dissection of artery of upper extremity
G726.00	107998	Dissection of renal artery
G727.00	105917	Dissection of iliac artery
G728.00	105117	Dissection of artery of lower extremity
G72y500	38732	Aneurysm of splenic artery
G72y500	38732	Aneurysm of splenic artery
G72y900	57135	Aneurysm of inferior mesenteric artery
G72yA00	27389	Aneurysm of hepatic artery
G72yB00	59536	Aneurysm of other visceral artery
G73..00	5943	Other peripheral vascular disease
G73..11	5702	Peripheral ischemic vascular disease
G73..12	1826	Ischaemia of legs
G73..13	6827	Peripheral ischaemia
G730000	1002	Raynaud's disease
G730100	5595	Raynaud's phenomenon
G730z00	39097	Raynaud's syndrome NOS

Readcode	Medcode	Diagnosis
G731.00	34638	Thromboangiitis obliterans
G731000	23497	Buerger's disease
G731z00	67401	Thromboangiitis obliterans NOS
G732.00	9204	Peripheral gangrene
G733.00	98174	Ischemic foot
G734.00	105317	Peripheral arterial disease
G73y.00	38907	Other specified peripheral vascular disease
G73y000	34152	Diabetic peripheral angiopathy
G73y100	23871	Peripheral angiopathic disease EC NOS
G73yz00	4325	Other specified peripheral vascular disease NOS
G73z.00	3530	Peripheral vascular disease NOS
G73z000	1517	Intermittent claudication
G73z011	6853	Claudication
G73z012	101866	Vascular claudication
G73z100	15863	Spasm of peripheral artery
G73zz00	2760	Peripheral vascular disease NOS
G740.12	5650	Aortoiliac obstruction
G742400	2065	Embolism and thrombosis of the femoral artery
G742500	4539	Embolism and thrombosis of the popliteal artery
G742600	69232	Embolism and thrombosis of the anterior tibial artery
G742700	71860	Embolism and thrombosis of the dorsalis pedis artery
G742900	44835	Embolism and thrombosis of a leg artery NOS
G742z00	15302	Peripheral arterial embolism and thrombosis NOS
G74y000	54865	Embolism and/or thrombosis of the common iliac artery
G74y100	32634	Embolism and/or thrombosis of the internal iliac artery
G74y200	56919	Embolism and/or thrombosis of the external iliac artery
G74y300	27494	Embolism and thrombosis of the iliac artery unspecified
G76z200	9554	Popliteal artery occlusion
Gyu7000	100579	[X]Atherosclerosis of other arteries
Gyu7100	102725	[X]Aortic aneurysm of unspecified site, ruptured
Gyu7200	102719	[X]Aortic aneurysm of unspecified site, nonruptured
Gyu7400	73961	[X]Other specified peripheral vascular diseases
J42..00	29276	Vascular insufficiency of the intestine
J420.00	37935	Acute intestinal vascular insufficiency
J420z00	35752	Acute intestinal vascular insufficiency NOS
J421.00	44030	Chronic intestinal vascular insufficiency
J421z00	61393	Chronic intestinal vascular insufficiency NOS
J42z.00	64368	Intestinal vascular insufficiency NOS
M271.12	6308	Ischemic leg ulcer
M271000	24327	Ischemic ulcer diabetic foot
M271300	11624	Arterial leg ulcer
M271400	8801	Mixed venous and arterial leg ulcer
P769000	8511	Renal artery stenosis
R055000	14796	[D]Failure of peripheral circulation
R055011	30484	[D]Peripheral circulatory failure
SP01200	96744	Mechanical complication of carotid artery bypass

ICD 10 codes for PAD

ICD_10	Diagnosis
I70.0	Atherosclerosis of aorta
I70.1	Atherosclerosis of renal artery
I70.2	Atherosclerosis of arteries of extremities
I70.8	Atherosclerosis of other arteries
I70.9	Generalized and unspecified atherosclerosis
I72.0	Aneurysm and dissection of carotid artery
I72.3	Aneurysm and dissection of iliac artery
I72.4	Aneurysm and dissection of artery of lower extremity
I73.9	Peripheral vascular disease, unspecified
I74.0	Arterial embolism and thrombosis

OPCS 4.6 codes for PAD

OPCS	Procedure
L481	Emergency replacement of aneurysmal common iliac artery by anastomosis of aorta to common iliac artery
L482	Emergency replacement of aneurysmal iliac artery by anastomosis of aorta to external iliac artery
L483	Emergency replacement of aneurysmal artery of leg by anastomosis of aorta to common femoral artery
L484	Emergency replacement of aneurysmal artery of leg by anastomosis of aorta to superficial femoral artery
L485	Emergency replacement of aneurysmal iliac artery by anastomosis of iliac artery to iliac artery
L486	Emergency replacement of aneurysmal artery of leg by anastomosis of iliac artery to femoral artery
L501	Emergency bypass of common iliac artery by anastomosis of aorta to common iliac artery NEC
L502	Emergency bypass of iliac artery by anastomosis of aorta to external iliac artery NEC
L503	Emergency bypass of artery of leg by anastomosis of aorta to common femoral artery NEC
L504	Emergency bypass of artery of leg by anastomosis of aorta to deep femoral artery NEC
L505	Emergency bypass of iliac artery by anastomosis of iliac artery to iliac artery NEC
L506	Emergency bypass of artery of leg by anastomosis of iliac artery to femoral artery NEC
L532	Open embolectomy of iliac artery
L561	Emergency replacement of aneurysmal femoral artery by anastomosis of femoral artery to femoral artery
L562	Emergency replacement of aneurysmal femoral artery by anastomosis of femoral artery to popliteal artery using prosthesis
L563	Emergency replacement of aneurysmal femoral artery by anastomosis of femoral artery to popliteal artery using vein graft
L564	Emergency replacement of aneurysmal femoral artery by anastomosis of femoral artery to tibial artery using prosthesis
L565	Emergency replacement of aneurysmal femoral artery by anastomosis of femoral artery to tibial artery using vein graft
L566	Emergency replacement of aneurysmal femoral artery by anastomosis of femoral artery to peroneal artery using prosthesis
L567	Emergency replacement of aneurysmal femoral artery by anastomosis of femoral artery to peroneal artery using vein graft
L581	Emergency bypass of femoral artery by anastomosis of femoral artery to femoral artery NEC
L582	Emergency bypass of femoral artery by anastomosis of femoral artery to popliteal artery using prosthesis NEC
L583	Emergency bypass of femoral artery by anastomosis of femoral artery to popliteal artery using vein graft NEC
L584	Emergency bypass of femoral artery by anastomosis of femoral artery to tibial artery using prosthesis NEC
L585	Emergency bypass of femoral artery by anastomosis of femoral artery to tibial artery using vein graft NEC
L586	Emergency bypass of femoral artery by anastomosis of femoral artery to peroneal artery using prosthesis NEC
L587	Emergency bypass of femoral artery by anastomosis of femoral artery to peroneal artery using vein graft NEC
L632	Percutaneous transluminal embolectomy of femoral artery
L633	Percutaneous transluminal embolisation of femoral artery
L161	Emergency bypass of aorta by anastomosis of axillary artery to femoral artery
L162	Bypass of aorta by anastomosis of axillary artery to femoral artery NEC
L163	Bypass of aorta by anastomosis of axillary artery to bilateral femoral arteries
L168	Other specified extra-anatomic bypass of aorta
L169	Unspecified extra-anatomic bypass of aorta

OPCS	Procedure
L181	Emergency replacement of aneurysmal segment of ascending aorta by anastomosis of aorta to aorta
L182	Emergency replacement of aneurysmal segment of thoracic aorta by anastomosis of aorta to aorta NEC
L183	Emergency replacement of aneurysmal segment of suprarenal abdominal aorta by anastomosis of aorta to aorta
L184	Emergency replacement of aneurysmal segment of infrarenal abdominal aorta by anastomosis of aorta to aorta
L185	Emergency replacement of aneurysmal segment of abdominal aorta by anastomosis of aorta to aorta NEC
L186	Emergency replacement of aneurysmal bifurcation of aorta by anastomosis of aorta to iliac artery
L188	Other specified emergency replacement of aneurysmal segment of aorta
L189	Unspecified emergency replacement of aneurysmal segment of aorta
L191	Replacement of aneurysmal segment of ascending aorta by anastomosis of aorta to aorta NEC
L192	Replacement of aneurysmal segment of thoracic aorta by anastomosis of aorta to aorta NEC
L193	Replacement of aneurysmal segment of suprarenal abdominal aorta by anastomosis of aorta to aorta NEC
L194	Replacement of aneurysmal segment of infrarenal abdominal aorta by anastomosis of aorta to aorta NEC
L195	Replacement of aneurysmal segment of abdominal aorta by anastomosis of aorta to aorta NEC
L196	Replacement of aneurysmal bifurcation of aorta by anastomosis of aorta to iliac artery NEC
L198	Other specified other replacement of aneurysmal segment of aorta
L199	Unspecified other replacement of aneurysmal segment of aorta
L201	Emergency bypass of segment of ascending aorta by anastomosis of aorta to aorta NEC
L202	Emergency bypass of segment of thoracic aorta by anastomosis of aorta to aorta NEC
L203	Emergency bypass of segment of suprarenal abdominal aorta by anastomosis of aorta to aorta NEC
L204	Emergency bypass of segment of infrarenal abdominal aorta by anastomosis of aorta to aorta NEC
L205	Emergency bypass of segment of abdominal aorta by anastomosis of aorta to aorta NEC
L206	Emergency bypass of bifurcation of aorta by anastomosis of aorta to iliac artery NEC
L208	Other specified other emergency bypass of segment of aorta
L209	Unspecified other emergency bypass of segment of aorta
L211	Bypass of segment of ascending aorta by anastomosis of aorta to aorta NEC
L212	Bypass of segment of thoracic aorta by anastomosis of aorta to aorta NEC
L213	Bypass of segment of suprarenal abdominal aorta by anastomosis of aorta to aorta NEC
L214	Bypass of segment of infrarenal abdominal aorta by anastomosis of aorta to aorta NEC
L215	Bypass of segment of abdominal aorta by anastomosis of aorta to aorta NEC
L216	Bypass of bifurcation of aorta by anastomosis of aorta to iliac artery NEC
L218	Other specified other bypass of segment of aorta
L219	Unspecified other bypass of segment of aorta
L231	Plastic repair of aorta and end to end anastomosis of aorta
L232	Plastic repair of aorta using subclavian flap
L233	Plastic repair of aorta using patch graft
L234	Release of vascular ring of aorta
L235	Revision of plastic repair of aorta
L236	Plastic repair of aorta and insertion of tube graft
L251	Endarterectomy of aorta and patch repair of aorta
L252	Endarterectomy of aorta NEC
L253	Open embolectomy of bifurcation of aorta
L254	Operations on aneurysm of aorta NEC
L261	Percutaneous transluminal balloon angioplasty of aorta
L262	Percutaneous transluminal angioplasty of aorta NEC
L263	Percutaneous transluminal embolectomy of bifurcation of aorta
L265	Percutaneous transluminal insertion of stent into aorta
L266	Transluminal aortic stent graft with fenestration NEC
L267	Transluminal aortic branched stent graft NEC
L268	Other specified transluminal operations on aorta
L269	Unspecified transluminal operations on aorta
L271	Endovascular insertion of stent graft for infrarenal abdominal aortic aneurysm
L272	Endovascular insertion of stent graft for suprarenal aortic aneurysm
L273	Endovascular insertion of stent graft for thoracic aortic aneurysm
L274	Endovascular insertion of stent graft for aortic dissection in any position
L275	Endovascular insertion of stent graft for aortic aneurysm of bifurcation NEC
L276	Endovascular insertion of stent graft for aorto-uniiliac aneurysm
L278	Other specified transluminal insertion of stent graft for aneurysmal segment of aorta

OPCS	Procedure
L279	Unspecified transluminal insertion of stent graft for aneurysmal segment of aorta
L281	Endovascular insertion of stent for infrarenal abdominal aortic aneurysm
L282	Endovascular insertion of stent for suprarenal aortic aneurysm
L283	Endovascular insertion of stent for thoracic aortic aneurysm
L284	Endovascular insertion of stent for aortic dissection in any position
L285	Endovascular insertion of stent for aortic aneurysm of bifurcation NEC
L286	Endovascular insertion of stent for aorto-uniiliac aneurysm
L288	Other specified transluminal operations on aneurysmal segment of aorta
L289	Unspecified transluminal operations on aneurysmal segment of aorta
L291	Replacement of carotid artery using graft
L292	Intracranial bypass to carotid artery NEC
L293	Bypass to carotid artery NEC
L294	Endarterectomy of carotid artery and patch repair of carotid artery
L295	Endarterectomy of carotid artery NEC
L311	Percutaneous transluminal angioplasty of carotid artery
L373	Endarterectomy of subclavian artery and patch repair of subclavian artery
L374	Endarterectomy of subclavian artery NEC
L391	Percutaneous transluminal angioplasty of subclavian artery
L395	Percutaneous transluminal insertion of stent into subclavian artery
L398	Other specified transluminal operations on subclavian artery
L399	Unspecified transluminal operations on subclavian artery
L411	Plastic repair of renal artery and end to end anastomosis of renal artery
L412	Bypass of renal artery
L414	Endarterectomy of renal artery
L431	Percutaneous transluminal angioplasty of renal artery
L435	Percutaneous transluminal insertion of stent into renal artery
L453	Endarterectomy of visceral branch of abdominal aorta and patch repair of visceral branch of abdominal aorta NEC
L454	Endarterectomy of visceral branch of abdominal aorta NEC
L458	Other specified reconstruction of other visceral branch of abdominal aorta
L459	Unspecified reconstruction of other visceral branch of abdominal aorta
L461	Open embolectomy of visceral branch of abdominal aorta NEC
L462	Open embolization of visceral branch of abdominal aorta NEC
L471	Percutaneous transluminal angioplasty of visceral branch of abdominal aorta NEC
L474	Percutaneous transluminal insertion of stent into visceral branch of abdominal aorta NEC
L478	Other specified transluminal operations on other visceral branch of abdominal aorta
L479	Unspecified transluminal operations on other visceral branch of abdominal aorta
L488	Other specified emergency replacement of aneurysmal iliac artery
L489	Unspecified emergency replacement of aneurysmal iliac artery
L491	Replacement of aneurysmal common iliac artery by anastomosis of aorta to common iliac artery NEC
L492	Replacement of aneurysmal iliac artery by anastomosis of aorta to external iliac artery NEC
L493	Replacement of aneurysmal artery of leg by anastomosis of aorta to common femoral artery NEC
L494	Replacement of aneurysmal artery of leg by anastomosis of aorta to superficial femoral artery NEC
L495	Replacement of aneurysmal iliac artery by anastomosis of iliac artery to iliac artery NEC
L496	Replacement of aneurysmal artery of leg by anastomosis of iliac artery to femoral artery NEC
L498	Other specified other replacement of aneurysmal iliac artery
L499	Unspecified other replacement of aneurysmal iliac artery
L508	Other specified other emergency bypass of iliac artery
L509	Unspecified other emergency bypass of iliac artery
L511	Bypass of common iliac artery by anastomosis of aorta to common iliac artery NEC
L512	Bypass of iliac artery by anastomosis of aorta to external iliac artery NEC
L513	Bypass of artery of leg by anastomosis of aorta to common femoral artery NEC
L514	Bypass of artery of leg by anastomosis of aorta to deep femoral artery NEC
L515	Bypass of iliac artery by anastomosis of iliac artery to iliac artery NEC
L516	Bypass of artery of leg by anastomosis of iliac artery to femoral artery NEC
L518	Other specified other bypass of iliac artery
L519	Unspecified other bypass of iliac artery

OPCS	Procedure
L521	Endarterectomy of iliac artery and patch repair of iliac artery
L522	Endarterectomy of iliac artery NEC
L528	Other specified reconstruction of iliac artery
L529	Unspecified reconstruction of iliac artery
L531	Repair of iliac artery NEC
L533	Operations on aneurysm of iliac artery NEC
L538	Other specified other open operations on iliac artery
L539	Unspecified other open operations on iliac artery
L541	Percutaneous transluminal angioplasty of iliac artery
L542	Percutaneous transluminal embolectomy of iliac artery
L543	Arteriography of iliac artery
L544	Percutaneous transluminal insertion of stent into iliac artery
L548	Other specified transluminal operations on iliac artery
L549	Unspecified transluminal operations on iliac artery
L568	Other specified emergency replacement of aneurysmal femoral artery
L569	Unspecified emergency replacement of aneurysmal femoral artery
L571	Replacement of aneurysmal femoral artery by anastomosis of femoral artery to femoral artery NEC
L572	Replacement of aneurysmal femoral artery by anastomosis of femoral artery to popliteal artery using prosthesis NEC
L573	Replacement of aneurysmal femoral artery by anastomosis of femoral artery to popliteal artery using vein graft NEC
L574	Replacement of aneurysmal femoral artery by anastomosis of femoral artery to tibial artery using prosthesis NEC
L575	Replacement of aneurysmal femoral artery by anastomosis of femoral artery to tibial artery using vein graft NEC
L576	Replacement of aneurysmal femoral artery by anastomosis of femoral artery to peroneal artery using prosthesis NEC
L577	Replacement of aneurysmal femoral artery by anastomosis of femoral artery to peroneal artery using vein graft NEC
L578	Other specified other replacement of aneurysmal femoral artery
L579	Unspecified other replacement of aneurysmal femoral artery
L588	Other specified other emergency bypass of femoral artery
L589	Unspecified other emergency bypass of femoral artery
L591	Bypass of femoral artery by anastomosis of femoral artery to femoral artery NEC
L592	Bypass of femoral artery by anastomosis of femoral artery to popliteal artery using prosthesis NEC
L593	Bypass of femoral artery by anastomosis of femoral artery to popliteal artery using vein graft NEC
L594	Bypass of femoral artery by anastomosis of femoral artery to tibial artery using prosthesis NEC
L595	Bypass of femoral artery by anastomosis of femoral artery to tibial artery using vein graft NEC
L596	Bypass of femoral artery by anastomosis of femoral artery to peroneal artery using prosthesis NEC
L597	Bypass of femoral artery by anastomosis of femoral artery to peroneal artery using vein graft NEC
L598	Other specified other bypass of femoral artery
L599	Unspecified other bypass of femoral artery
L601	Endarterectomy of femoral artery and patch repair of femoral artery
L602	Endarterectomy of femoral artery NEC
L603	Profundoplasty of femoral artery and patch repair of deep femoral artery
L604	Profundoplasty of femoral artery NEC
L608	Other specified reconstruction of femoral artery
L609	Unspecified reconstruction of femoral artery
L631	Percutaneous transluminal angioplasty of femoral artery

Supplementary Table S8: CPRD diagnosis codes for important co-morbidities

Baseline characteristics	Medcodes (CPRD)
High bleeding risk	621,712,880,1044,1105,1201,1354,1735,1786,1819,1867,2044,2629,2814,2832,2833,2883,3039,3535,3588,3589,3822,3872,4006,4273,4635,4942,5051,5198,5365,5422,5632,5682,5981,6554,6569,6574,6684,6872,6960,7194,7285,7733,7912,8181,8742,9143,9454,9503,9571,9696,9759,9761,10118,10534,10625,10779,11053,11061,11124,11430,11678,11698,11718,11950,13564,13572,15257,15304,15464,15517,16034,16068,16114,16366,16395,16419,16420,16445,16521,16554,16800,16848,17027,17218,17345,17560,17767,17825,18001,18012,18269,18281,18478,18604,18617,18625,18677,18912,19201,19221,19271,19412,19532,20181,20266,20284,20828,20857,21739,21799,22176,22463,22651,22706,23532,23580,23601,23813,24324,24424,24729,24989,25438,26065,26198,27289,27389,27563,27661,28077,28109,28144,28314,28366,28573,28652,28763,28765,28807,29492,29702,29939,30045,30054,30132,30202,30248,30403,30415,30655,31055,31060,31166,31395,31595,31805,31876,31941,32446,33360,33613,33843,33895,34125,34466,35285,35315,35529,36178,36390,36583,36666,37250,37550,37772,37823,38137,38180,38304,38732,38754,38851,39575,40338,40430,40524,40787,41171,41520,41910,42283,42331,42421,42581,43451,44089,44258,44581,44637,44740,45000,45214,45304,45421,45450,45521,45698,45734,45897,45962,46152,46316,46479,46545,46726,46938,47195,47203,47497,48085,48086,48149,48181,48730,48951,49374,49474,49791,49901,50097,50260,50678,50746,50929,51504,51717,52186,52358,52549,52896,52968,53126,53810,53999,54005,55153,55166,55419,55604,56007,56200,56664,57135,57309,57315,57456,57958,58545,58691,58698,58757,58794,58906,59141,59375,59492,59536,59538,59671,59812,60341,60346,60692,60879,61062,62038,62061,62342,62587,62741,62795,63059,63173,63582,63620,63903,63910,63920,64451,64859,65029,65241,65745,65976,66823,66907,67026,67197,68333,68624,68641,69847,69892,70260,70456,71034,71139,71197,71253,71403,71783,71829,71881,71897,72062,72299,72503,73139,73471,86065,87869,88788,89150,89355,89456,90773,91467,91887,92986,93083,93267,93432,93436,93537,94146,94155,94351,94397,94408,94491,94806,95170,95381,95577,96225,96562,96622,96628,96630,96717,96756,97645,97937,99362,100733,101195,101379,101797,101824,102134,102306,102719,102725,103431,103544,103840,103936,104124,104146,105179,105621,105742,105760,105868,106330,106975,107188,107220,107440,108193,108345,108668,108759,109250,109538,110095,110244,111236,4107,4917,7862,17326,17734,18411,28914,43418,53980,96677,1642
Chronic Kidney Disease	350,512,2994,2996,4503,5475,6712,8037,8330,11773,12479,12566,12585,15917,20073,20196,20629,22252,25394,30735,30739,36442,44422,45160,46145,46438,53852,53940,56852,59018,59031,59315,60302,60446,60498,60743,61930,63038,63502,64828,66714,69266,69679,69760,71271,72336,72962,72964,88494,88597,94793,94965,95122,95123,95145,95175,95176,95177,95178,95179,95180,95188,95405,95406,95408,95422,95508,95571,96347,97587,97683,98888,99160,99312,100633,101124,101736,101756,101912,104586,104619,104719,104963,105143,105151,105919,106720,106860,106975,107082,107188,107260,107719,107746,107900,108116,108213,108423,108699,108759,108785,109135,109657,109809,109884,109904,109905,109945,109963,109980,109981,109990,110051,110072,110095,110467,110626,110976,111103
Hypertension	204,351,799,1894,2666,3425,3712,3979,4344,4372,4444,4668,5215,5513,6702,7057,7329,8296,8574,8732,8857,10818,10961,10976,11056,12680,12948,13186,13188,15106,15377,16059,16173,16292,16565,18057,18482,18590,18765,19070,20497,21660,21826,21837,22333,24127,25371,27511,27634,28684,28828,28874,29310,30770,30776,31117,31127,31175,31341,31387,31464,31755,31816,32423,32976,34108,34744,37086,39649,41634,42229,43220,43935,44350,45149,50157,51635,52127,52427,57288,57987,59383,61166,61660,62718,63000,63164,63260,63466,67232,68659,69753,72226,72668,73293,83473,85944,95334,95359,97533,98230,99259,101649,102406,102458,103046,105274,105316,105371,105480,105487,105938,105989,106279,107704,108136,109611,109771,109797,109942,110631
Diabetes Mellitus	6813,7045,17236,28622,18766,54846,46533,12703,34528,3550,13070,608,17886,13067,32619,66475,61470,13057,12682,47341,17478,17846,42217,55140,63412,47032,57723,50937,19381,47058,47011,93704,93657,93870,18747,12247,95094,97809,95093,94956,57389,38103,32739,38129,2379,10824,95813,9974,46521,12507,9145,30648,6430,54601,11930,11094,95553,95159,94955,97281,9897,13197,26603,22130,13194,13195,12030,31240,31141,13192,20900,26605,94186,94011,93390,93491,93529,93631

Baseline characteristics	Medcodes (CPRD)
	,93854,31241,28574,11041,11348,45250,8618,58133,68546,91164,94699,68818,38130,97824,67664,85660,24490,1038,53200,40023,42567,93922,69748,67853,70448,69124,1647,18505,17858,24423,46963,61344,21983,49276,52283,49146,61829,52104,26855,60107,97474,44443,51957,68390,60499,6509,38161,41049,6791,46850,45914,31310,63017,97446,56448,95992,24694,41716,57621,66872,44440,42729,70766,44260,17545,64446,65616,62352,39809,60208,18230,98392,1549,12455,51261,47582,47649,98071,42831,47650,91942,45276,43921,49949,54600,18683,93878,98704,69993,18387,95343,93875,35288,72702,40682,96235,97849,69676,62613,68105,46301,91943,10418,39070,49554,93468,18642,54008,30323,30294,10692,62209,40837,66145,22871,97894,55239,68792,50960,38076,43493,69043,32359,83532,14803,14889,506,54856,43139,68843,35105,41389,39317,63357,33807,56803,4513,5884,17859,18219,52303,50225,18209,50429,59725,70316,55842,67905,45919,62146,34912,55075,65704,40401,62107,46150,17262,58604,42762,8403,24458,45913,29979,72320,50813,45467,47409,59365,64571,24836,43785,56268,61071,69278,48192,44779,54212,54899,60699,24693,18143,49869,40962,47816,66965,18278,37648,18264,36633,46624,36695,59991,95636,758,22884,18777,57278,47321,34268,98616,65267,43227,49074,91646,12736,18496,49655,25627,47315,47954,53392,62674,95351,18425,50527,12640,46917,98723,44982,93727,37806,59253,35385,1407,64668,34450,26054,60796,18390,85991,32627,51756,25591,63690,63371,63762,50609,25041,11551,26108,95539,51697,96506,61122,67212,22487,94383,93380,32193,21689,13078,13074,22967,9835,47144,11433,11129,13099,13103,13097,13101,13102,13108,47328,52041,52630,27921,17095,26664,18056,26666,31157,31171,35316,26667,31156,31172,35116,62384,49640,7563,1684,8842,13069,38078,20696,13196,53238,16490,13071,2378,9013,2478,22023,43951,17869,29041,55123,12506,12675,8836,6125,18167,12307,28769,50175,46577,26604,25636,22823,10977,90301,66274,28873,69152,83485,96010,95994,49884,18311,19739,61021,11599,36798,17817,61670,24363,11471,12213,8414,12483,28856,7059,35321,11677,11018,18662,47370,64142,18824,12262,58159,58639,52237,35383,711,38986,50972,1682,38617,42505,21482,72345,15690,59288,65062,16502,2475,13279,35107,33254,47377,34283,16230,59903,7795,16491,61523,22573,35399,32403,32556,65025,46290,64449,52236,66675,33969,43453,43857,33343,10098,70821,45491,64283,64357,11848,23479,52212,41686,17067,44033,17247,31790,5002,2342,48078,35785,24571,39420,2340,37315,1323,7069,3286,2986,10099,3837,47584,10755,30477,65463,11626,17313,10659,34152,2471,55431,7328,24327,11663,9881,18142,57333,27891,21472,53634,31053,68928,61210,65684,10642,70073,16881,19203

Supplementary Table S9: Codes for important outcomes (Read codes + ICD 10 codes)

Outcomes	CPRD Read codes (Medcodes)	HES ICD-10 codes
Myocardial infarction	241,1204,1677,1678,2491,3704,5387,8935,9276,9413,9507,10562,11983,12139,12229,13566,13571,14658,14897,14898,17689,17872,18842,23579,23892,27951,27977,28736,29553,29643,29758,30330,30421,32272,32854,34803,36423,38609,39449,40429,41221,45809,46017,59940,61670,63467,68401,69474,72562,96838,99991,106812,107406,109035	I21.0,I21.1,I21.2,I21.3,I21.4,I21.9,I22.0,I22.1,I22.8,I22.9,I23.0,I23.1,I23.2,I23.3,I23.4,I23.5,I23.6,I23.8,I24.0
Ischemic Stroke	5363,6155,33543,39403,,40758,53745,91627,94482,1298,1469,5185,5871,6116,6228,6253,6305,7138,7780,8443,10792,10962,11039,11074,12833,17322,18686,18687,19348,28753,31218,32959,34135,34245,34375,42248,47642,51465,52246,55351,56279,56458,57183,66873,70536,89913,93459,95347,98145	I63.0,I63.1,I63.2,I63.3,I63.4,I63.5,I63.8,I63.9
Hospitalisation for bleeding		D699,H313,H356,H431,I312,I60.0,I60.1,I60.2,I60.3,I60.4,I60.5,I60.6,I60.7,I60.8,I60.9,I600,I601,I602,I603,I604,I605,I606,I607,I608,I609,I61.0,I61.1,I61.2,I61.3,I61.4,I61.5,I61.6,I61.8,I61.9,I610,I611,I612,I613,I614,I615,I616,I618,I619,I62,I62.0,I62.1,I62.9,I620,I621,I629,I690,I691,I692,I713,I715,I718,J942,K226,K250,K252,K254,K256,K260,K262,K264,K266,K270,K272,K274,K276,K280,K282,K283,K284,K286,K290,K625,K661,K920,K921,K922,M250,N02,N421,N836,N837,N857,N897,N923,N924,N93,N930,N938,N939,N950,O051,O20,O208,O209,O224,O670,O678,O679,O872,O902,R040,R041,R042,R048,R049,R31,R58,S064,S065,S066,T792,T810,K29.0,K62.5,K92.0,K92.1,K92.2

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