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a nationwide cohort study on cardiovascular morbidity and medical cardioprotective therapy

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Temporal trends in abdominal aortic aneurysmal disease - A nationwide cohort study on cardiovascular morbidity and medical cardioprotective therapy

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Short Title: Cardiovascular morbidity and medical prevention in AAA

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Abstract

Background: Abdominal aortic aneurysmal disease is associated with increased risk of cardiovascular morbidity and death, which potentially can be reduced with cardioprotective medical therapy.

Aim: To study temporal trends in prevalence and incidence of cardiovascular comorbidity as well as use of medical cardioprotective treatment in patients diagnosed with abdominal aortic aneurysmal disease.

Methods: This was a population-based cohort study based on data from national health registries, including all patients diagnosed with abdominal aortic aneurysms between 1998 and 2018. Data were stratified into four time-periods (1999-2003, 2004-2008, 2009-2013, and 2014-2018) to illustrate trends over time. Outcomes measures were: 1. cardiovascular comorbidity and medical cardioprotective therapy at time of diagnosis, 2. new admissions for atherosclerotic cardiovascular disease, and 3. all-cause mortality after two-year follow-up.

Results: The study-cohort included 33,296 individuals. Mean age was 74 years. Prevalence of atherosclerotic cardiovascular comorbidity at diagnosis decreased from 41.5% to 32.6%. Use of statins increased from 17.9% to 66.9%, antiplatelets from 45.6% to 63.3%, and combined therapy with both antiplatelets and statins from 11.3% to 44.8%, and from 12.1% to 50.7% when anticoagulant therapy was included. Developments in medication use plateaued after 2013. Prevalence and incidence of atherosclerotic cardiovascular disease decreased through all four time periods. The same applied to all-cause mortality, which decreased from 24.3 to 12.4 deaths (per 100 person-years).

Conclusion: In patients diagnosed with abdominal aortic aneurysm, cardiovascular comorbidity at diagnosis, risk of future cardiovascular events, and all-cause mortality is

decreasing. Nevertheless, cardiovascular burden and mortality rates remain substantial, and medical cardioprotective therapy can be further improved.

Abstract wordcount: 255

Keywords: Abdominal aortic aneurysm, medical cardioprotective treatment, stroke, myocardial infarction, cardiovascular disease

Introduction

Abdominal aortic aneurysmal (AAA) disease is the cause of 1% of all deaths among individuals aged 65 years and older.[1,2] The estimated annual risk of cardiovascular death among patients with AAA is 3% compared with 0.8% in the general population.[3] Paradoxically, morbidity and mortality remains high, despite improvements in repair techniques and aneurysm-related survival.[4–7] The increased mortality is mediated principally through factors other than the aneurysmal disease itself, [8–10] primarily driven by ischemic heart disease (IHD), cerebrovascular disease (CeVD), and peripheral arterial disease (PAD).[3,9] Atherosclerotic vascular events and premature death can be reduced with preventive medical therapy.[9,11] Therefore, a major goal in AAA management, is risk factor modification and lifestyle changes. Cardioprotective medications, such as statins, aspirin, and antihypertensive agents, have been associated with a 20-35% lower risk of all-cause mortality among patients with AAA, irrespective of AAA repair. [9,12,13] Thus, a growing international consensus recommends blood pressure control and medical therapy with statins, antiplatelet, and antihypertensive agents at the time of AAA diagnosis (Figure 1).[4,14–17]

The aim of this study was to provide updated nationwide data on temporal changes in cardiovascular comorbidity, use of medical cardioprotective treatment at AAA diagnosis, and cardiovascular outcomes in patients diagnosed with AAA.

Methods

This population-based historical cohort study reports consecutive data on patients with AAA from registries covering the entire Danish population. All hospitals in Denmark have a compulsory registry policy, leading to virtually complete enrolment of the Danish population due to the unique personal registration number given to all citizens at birth or immigration.[18]

Data sources

Using the Danish National Patient Registry (DNPR), we identified all patients with a first diagnosis of AAA between 1999 and 2018, covering both in- and outpatient registrations. The DNPR has stored information on hospitalizations since 1977, and outpatient and emergency department visits at all hospitals in Denmark since 1995.[19] Data include Civil Personal Registry numbers, dates of admission and discharge, and up to 20 diagnoses coded by the International Classification of Diseases (ICD-10). Data on medication claims were retrieved form the Danish National Prescription Registry,[20] which has detailed information on the purchase date, Anatomical Therapeutic Chemical classification code, package size, and dose for every prescription claim since 1994. Data on patient characteristics such as age, sex, and vital status were extracted from the Civil Registration Registry.[19] Because of the non-anonymized nature of the data collected for this study, requests to access the dataset from third parties are not allowed according to Danish data safety regulations.

Ethics

In Denmark, approval from an ethics committee is not required for registry-based studies in which specific individuals cannot be identified. The study was performed in compliance with

the General Data Protection Regulation and the North Denmark Region's record of processing activities (project no. 2017-40). Data were provided by the Danish Health Data Authority.

Study population

The first diagnosis of AAA was identified either by a primary or secondary discharge diagnosis (in- and outpatient ICD-10 codes: I713, I714), in the DNPR (index date). Previous validation studies have reported a positive predictive value of the AAA diagnosis in the DNPR of >98%.[21] Patients who had not resided in Denmark within the year before AAA diagnosis were excluded. Patients aged <50 years were excluded to account for patients with potential erroneous diagnosis of AAA and to exclude patients with severe connective tissue disease, which has a different aetiology than degenerative AAA.

Comorbidity and cardioprotective treatment

To assess medical cardioprotective treatment at the time of AAA diagnosis, we included baseline medication on antiplatelets, anticoagulants, statins, and antihypertensives. We also assessed the total use of antithrombotic therapy, defined as either anticoagulation or antiplatelet therapy. Patients on anticoagulant therapy were included to provide the most accurate picture of trends, as a chronic indication for anticoagulants in many cases overrules the indication for antiplatelet therapy in patients with AAA. Patients were defined as receiving recommended treatment if they claimed a prescription of both antiplatelet and statin therapy. Antihypertensive treatment was reported separately, as this is only recommended in AAA patients with hypertension in Denmark.

To examine changes in prevalent comorbidities, we extracted data on comorbid conditions requiring secondary healthcare, recorded within five years preceding AAA diagnosis, including: atherosclerotic vascular disease (CeVD, IHD and PAD), hypertension, chronic pulmonary disease, chronic kidney disease, heart failure, atrial fibrillation, venous thromboembolism, heart valve replacement, diabetes mellitus, rheumatic disorders, and malignancy (Supplemental Table I).

For specification of variables and ICD-10/ATC codes used for analysis, please see Supplemental Table 1.

Outcomes

Patients were followed for up to two years after the index date or until administrative censoring, December 31, 2018, for the occurrence of adverse cardiovascular outcomes (new admissions for CeVD, IHD and PAD), and death of all causes. To avoid repeated coding of prevalent conditions, cardiovascular outcomes were based on diagnosis in the primary position for hospitalized patients recorded in the DNRP.

Statistical analysis

To illustrate changes over time, patient inclusion was stratified into four time periods; 'Period 1' (1999–2003), 'Period 2' (2004–2008), 'Period 3' (2009-2013), and 'Period 4' (2014–2018) and applied as study exposure groups. Age- and sex-standardized incidence rates of AAA were calculated by dividing the total number of incident patients with AAA per year by the mid-year number of residents in Denmark within the same time period. Descriptive statistics were used to summarize changes in demographics and comorbidities. Categorical data were reported as percentages and continuous data as medians with accompanying interquartile

ranges (IQR). To distinguish between prevalent use and initiation (new use) of cardioprotective medicine after AAA diagnosis, we conducted a stratified analysis according to whether a prescription was filled in the 365 days before diagnosis or exclusively in the 90 days after (i.e., treatment initiation after diagnosis). Further, we conducted a subgroup analysis on medical treatment, stratified according to presence of atherosclerotic cardiovascular disease (CeVD, IHD and PAD) at the time of AAA diagnosis.

Time-to-event analyses were applied to calculate incidence rates of new atherosclerotic vascular admissions during follow-up. Kaplan-Meier estimates were used to describe risk of all-cause mortality. Assuming independent censoring, crude Aalen-Johansen estimates were used to depict cumulative incidence curves for each type of atherosclerotic vascular disease assuming death as a competing risk. Outcomes were reported as cumulative incidence proportions and incidence rates (events/100 person-years) at two-years follow-up. All-cause mortality stratified by diagnosis (ruptured (DI713) or non-ruptured (DI714) AAA) was included as a secondary analysis.

All analyses were performed using SAS (version 9.4) and STATA/MP (version 16).

Results

Between 1999 and 2018, 33,296 individuals were diagnosed with AAA in Denmark, with an estimated population of 5.8 million. The AAA numbers increased from 5,912 in Period 1 (1999-2003) to 9,998 in Period 4 (2014-2018) (Table 1). The age- and sex-standardized incidence of AAA (per 100,000 residents) increased from 68.2 in Period 1 to 84.7 in Period 4, with a peak incidence of 93.6 in period 3 (2009-2013). The median age at diagnosis was 73 years in Period 1 and 74 years in Period 4; approximately 25% were females in all four periods. The proportion of patients first diagnosed with ruptured AAA decreased from 19.9% in Period 1 to 8.3% in Period 4 (Table 1).

Trends in comorbidity

The proportion of AAA patients with at least one comorbid condition ranged between 63.0% and 65.6% throughout the study period. The proportion of patients with any atherosclerotic cardiovascular disease (CeVD, IHD, PAD) decreased from 41.5% in Period 1 to 32.6% in Period 4 (Table 1), primarily caused by decreases in prevalence of IHD (24.3% to 19.2%) and PAD (17.2% to 11.0%). Increases were observed in the prevalence of hypertension (17.9% to 30.8%), diabetes (5.2% to 8.7%), atrial fibrillation (9.6% to 12.5%), and cancer (8.8% to 13.9%), while the prevalence of other comorbid conditions, including CeVD, remained unchanged.

Trends in medical treatment

The use of medical cardioprotective therapy at the time of AAA diagnosis increased from 1999 to 2018, both overall and for new users commencing treatment within 90 days after AAA diagnosis (Table 2). The use of antihypertensives increased from 71.3% in period 1 to

78.5% in Period 4. Most patients were prevalent users, while treatment initiation after AAA diagnosis ranged between 5.0% and 7.7%. Statin use increased from 17.9% in Period 1 to 66.9% in Period 4, while treatment initiation after AAA diagnosis remained modest (2.4-13.5%). The use of antiplatelet therapy increased from 45.6% to 68.7% between Period 1 and 3, with a small decrease in Period 4 to 63.3%. The proportion of new users continuously increased from 7.7% to 16.2%. When we included OAC, the overall use of antithrombotic therapy (prescription claim of either antiplatelet therapy or OAC) increased from 51.1% in Period 1 to 76.5% in Period 4. Overall, the proportion of patients receiving recommended therapy with both antiplatelets and statins increased from 11.3% in Period 1 to 44.8% in Period 4, with a maximum of 49.0% in Period 3 (50.7% when all antithrombotics were included). Fewer than 10% of treatment-naïve patients started guideline-recommended therapy after AAA diagnosis. For all drug groups, no increases were observed between 2014 and 2018 (Period 4).

Use of cardioprotective therapy increased over time in all subgroups yet remained lower among patients with no prior atherosclerotic vascular disease compared to those with concomitant atherosclerosis (Figure 2A+B). Among patients with no history of atherosclerotic disease, use of antiplatelet therapy increased from 31.9% in Period 1 to 53.9% in Period 4, with a peak of 58.2% in Period 3, and 19.9% with treatment initiation after AAA diagnosis in Period 4 (Figure 2A). When OAC was included, antithrombotic therapy increased continuously from 36.3% to 66.0% (Figure 2B). In patients with concomitant atherosclerotic vascular disease, the use of antiplatelets increased from 64.8% in Period 1 to 82.8% in Period 4, with a peak of 86.8% in Period 3, and a maximum of 9% new users. Antithrombotic use increased continuously from 71.9% to 98.0% between Period 1 and 4. Statin use increased

from 8.9% to 60.3% in patients with no previous record of atherosclerotic vascular disease (14.3%% new users in Period 4) and from 30.6% to 82.2% in patients with atherosclerotic vascular disease (4.9% new users in Period 4). Among those with no history of atherosclerotic vascular disease, prevalence of patients receiving recommended therapy with both statins and antiplatelets never exceeded 40%. In contrast, cardioprotective treatment was more frequently used among patients with concomitant atherosclerosis. In this subgroup, 74.1% received both antiplatelets and statin in Period 4 (Figure 2A).

Trends in incidence of atherosclerotic vascular admissions and all-cause mortality

Incidence rates of new hospitalizations for atherosclerotic cardiovascular disease after AAA diagnosis was lower in each successive time period (Figure 3A). The largest difference over time was observed for IHD and PAD. For IHD, the incidence rate of new admissions was 6.2 (per 100 person-years) in Period 1 and 2.8 in Period 4, and for PAD, the incidence rates 3.8 in Period 1 and 1.7 in Period 4 (Table 3). Similarly, the cumulative all-cause mortality at two-year follow-up was lower in each successive time period (Figure 3B), with a change in rate from 24.3 in Period 1 to 12.4 in Period 4 (Table 3), despite higher patient age at diagnosis. The cumulative mortality differed according to presentation at diagnosis (ruptured, non-ruptured) (Figure 3B).

Discussion

In our 20-year study, the overall incidence of AAA increased, with a peak in 2009-2013, while the proportion of patients presenting with a primary diagnosis of ruptured AAA plummeted by more than 50%. The prevalence of concomitant atherosclerotic cardiovascular disease decreased over time. The rate of adverse atherosclerotic cardiovascular events leading to hospitalization and death of all causes also declined. Mortality, however, remained substantial. One in five patients diagnosed with AAA between 2014 and 2018 died within two years of diagnosis. This finding persisted even when excluding patients with ruptured AAA. Despite a consensus endorsing intensified medical therapy for these patients,[14,22] no further increase in utilization of in medical cardioprotective therapy was observed after 2013. Half of AAA patients still did not receive concomitant medical therapy with statin and antiplatelet (or any antithrombotic) therapy in Period 4.

We found a decreasing and consistently lower prevalence of comorbid atherosclerotic vascular disease at the time of AAA diagnosis than previously described.[3,9] The rate of new atherosclerotic events requiring hospitalization was 2.0 (per 100 person years) for CeVD, 2.8 for IHD, and 1.7 for PAD in Period 4. In comparison, the Danish Heart Association found hospitalization rates of 0.8 for CeVD, 1.0 for IHD, and 0.5 for PAD in 2018 in the general population of comparable age and sex (males, age group 65 -74 years).[23] Thus, atherosclerotic cardiovascular disease continues to be a major cause of long-term morbidity in patients with AAA, highlighting the importance of addressing cardiovascular risk management and prevention at time of AAA diagnosis.

Our findings of an increasing percentage of AAA patients receiving medical cardioprotective treatment at diagnosis from 1999 to 2013 support the trend described by Bahia et al. who examined general practice records of AAA patients in the UK.[9] For most AAA patients, the benefits of secondary cardioprotective treatment outweigh the costs and risk of side-effects associated with antiplatelet and statin treatment, regardless of comorbid atherosclerotic status and age.[9,11,13] Nevertheless, we discovered a plateau in the use of cardioprotective drugs in period 4 (2014-2018). These findings were consistent in patients with and without comorbid atherosclerotic vascular disease. Similar observations were made in the US and in several European countries in other patient groups with cardiovascular disease, suggesting a more general trend in cardiovascular preventive medicine.[24–27]

Study strengths and limitations

Our 20-year observation period may have included potential confounding factors, such as changes in availability of diagnostics, leading to increased opportunistic screening for AAA. This may partially explain the observed changes in incidence of AAA and a lower proportion presenting with ruptured AAA. Records in the Danish health registries are generally considered an accurate depiction of clinical diagnosis.[20,28] Still, there is a risk of misclassification and a risk of changes in coding behaviour over time, e.g., caused by more aggressive monitoring and stricter limits for blood pressure and lipid levels. This may explain the large increases in diagnosis of prevalent hypertension observed over time. Additionally, we used prescription data to estimate trends in medical cardioprotective therapy. As aspirin is also dispensed over the counter in Denmark, this may potentially have introduced underestimation of antiplatelet use. However, most low-dose aspirin (75-150 mg) are

dispensed by prescription (>90% in 2012[29]), and thus, retail aspirin use is considered to have only limited influence on observed trends. Further, causes of death could not be ascertained separately, leading to a potential underestimation of the true incidence of cardiovascular hospitalizations during follow-up. Another limitation of our study is the lack of data on smoking status, exercise, and body mass index. Factors, which may have influenced morbidity and all-cause mortality.[30]

This study provided nationwide, detailed, and unselected coverage of data, reflecting real-life clinical practice from health registries of high validity. Updated information was provided on comorbidity and medical treatment with no bias from loss to follow-up. We included all AAAs, independent of size and presentation (ruptured, non-ruptured AAA), thus providing a comprehensive picture of trends in morbidity and cardioprotective medical treatment at the time of AAA diagnosis.

Conclusion

The prevalence of concomitant atherosclerotic cardiovascular disease and the incidence of new atherosclerotic admissions after AAA diagnosis decreased over the 20-year study period. However, the burden of prevalent and incident IHD and PAD remained high compared to the general population. Efforts to intensify implementation of medical cardioprotective therapy has the potential to further reduce morbidity and enhance survival in patients with AAA.

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Disclosures

M. Søgaard has received consulting fees from Bayer. N. Eldrup has served as an investigator for Bayer, and has received fees for speaking engagement from Bayer, Amgen, and AstraZeneca. T.B. Larsen has served as an investigator for Janssen Scientific Affairs, LLC and Boehringer Ingelheim; Larsen has also participated in speaker panels for Bayer, Bristol-Myers Squibb, Pfizer, Roche Diagnostics, and Boehringer Ingelheim; Larsen has also received honoraria for consulting activities from Bayer, Boehringer Ingelheim, Bristol-Myers Squibb and Pfizer. T.B. Larsen's institution has received unrestricted funds for investigator-initiated research activities from Bayer, Pfizer, and Daiichi Sankyo. P. B. Nielsen has received fees for speaking engagements from Boehringer Ingelheim and BMS/Pfizer; fees for consulting from Bayer and Daiichi-Sankyo; and grant support from BMS/Pfizer and Daiichi-Sankyo Europe. All other authors declare no conflicts of interest.

Author contributions

CWN, MS, NE, TBL and SZG contributed to the conception or design of the work. CWN, MS, MJ, PBN contributed to the acquisition, analysis, or interpretation of data for the work. CWN drafted the manuscript. CWN, MS, NE, TBL, SZG and PBN critically revised the

manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy."

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Table 1. Demographics and comorbidity of study cohort stratified by time period

	Period 1 1999-2003	**Period 2 2004-2008**	**Period 3 2009-2013**	**Period 4 2014-2018**
Demographics, % (N)				
N	6009	7784	9602	9998
Age, median (IQR)	73 (67-79)	73 (68-79)	74 (68-79)	74 (69-80)
Female	24.7 (1458)	25.1 (1950)	23.8 (2281)	23.5 (2351)
Ruptured AAA	19.9 (1175)	15.2 (1180)	10.2 (978)	8.3 (828)
Any atherosclerotic cardiovascular disease	41.5 (2456)	40.7 (3169)	36.3 (3487)	32.6 (3264)
Cerebrovascular Disease	10.4 (613)	10.7 (832)	9.1 (875)	8.9 (887)
- Ischemic stroke	7.8 (459)	8.0 (620)	6.4 (617)	6.4 (635)
Ischemic Heart Disease	24.3 (1439)	24.5 (1910)	21.7 (2080)	19.2 (1916)
- Myocardial Infarction	7.8 (459)	7.0 (546)	6.0 (575)	5.3 (531)
Peripheral Arterial Disease	17.2 (1017)	15.0 (1168)	12.9 (1239)	11.0 (1102)
Comorbidity, other				
Hypertension	17.9 (1059)	26.8 (2084)	30.1 (2889)	30.8 (3084)
Diabetes	5.2 (308)	7.3 (571)	8.5 (819)	8.7 (867)
Heart Failure	9.9 (585)	9.6 (744)	8.1 (773)	7.9 (774)
Atrial Fibrillation	9.6 (559)	11.5 (892)	11.6 (1112)	12.5 (1251)
Chronic Pulmonary Disease	12.5 (740)	13.2 (1025)	13.4 (1288)	14.4 (1440)
Chronic Renal Disease	4.9 (290)	5.2 (405)	5.9 (571)	6.2 (617)
Rheumatic Disease	2.7 (157)	2.9 (227)	3.2 (308)	3.6 (362)
Cancer	8.8 (522)	10.8 (844)	12.8 (1233)	13.9 (1394)
Venous Thromboembolism	2.4 (141)	2.6 (201)	3.0 (285)	3.8 (381)
Mechanical Heart Valve	0.5 (29)	1.1 (84)	1.4 (132)	1.2 (124)

IQR – Inter quartile range, n – number, AAA –abdominal aortic aneurysm

Table 2. Proportion of AAA patients receiving medical therapy according to time periods

Treatment, % (N)	**Period 1 1999-2003** (n = 5912)	**Period 2 2004-2008** (n = 7784)	**Period 3 2009-2013** (n = 9602)	**Period 4 2014-2018** (n = 9998)
Any antiplatelet	**45.6 (2692)**	**59.5 (4633)**	**68.7 (6592)**	**63.3 (6333)**
- prevalent use	37.9 (2238)	47.9 (3731)	53.3 (5116)	47.1 (4714)
- new use	7.7 (454)	11.6 (902)	15.4 (1476)	16.2 (1619)
Any antithrombotic*	**51.1 (3022)**	**66.2 (4757)**	**76.2 (7314)**	**76.5 (7648)**
- prevalent use	41.7 (2468)	53.0 (4128)	59.1 (5672)	57.6 (5754)
- new use	9.4 (554)	13.2 (1026)	17.1 (1642)	18.9 (1894)
Statin	**17.9 (1058)**	**50.8 (3954)**	**68.2 (6550)**	**66.9 (6691)**
- prevalent use	15.5 (915)	39.4 (3069)	54.7 (5252)	55.7 (5568)
- new use	2.4 (143)	11.4 (885)	13.5 (1298)	11.2 (1123)
Any antihypertensive	**71.3 (4218)**	**77.7 (4393)**	**79.1 (7589)**	**78.5 (7839)**
- prevalent use	63.6 (3761)	69.6 (5419)	73.7 (7074)	73.5 (7344)
- new use	7.7 (457)	8.1 (632)	5.4 (515)	5.0 (495)
Recommended therapy†	**12.1 (716)**	**36.8 (2861)**	**51.9 (4983)**	**50.7 (5068)**
- prevalent use	11.2 (661)	30.9 (2402)	43.4 (4169)	42.9 (4289)
- new use	0.9 (55)	5.9 (459)	8.5 (814)	7.8 (779)

AAA – Abdominal Aortic Aneurysm, New use - Patients with first drug-redemption within 90 days after diagnosis of AAA, *Antithrombotic treatment with antiplatelet therapy or anticoagulant therapy, †Guideline-recommended therapy with any anti-thrombotic and statin therapy

Table 3. Incidence rates of all outcomes (incident cardiovascular admissions and all-cause mortality) at two-year follow-up.

	Period 1 **1999-2003**	**Period 2** **2004-2008**	**Period 3** **2009-2013**	**Period 4** **2014-2018**
Cerebrovascular disease	3.40 (285)	2.53 (370)	2.03 (324)	1.97 (279)
Ischemic stroke	2.59 (219)	1.61 (197)	1.33 (214)	1.17 (166)
Ischemic heart disease	6.20 (505)	4.94 (582)	3.82 (597)	2.77 (388)
Myocardial infarction	2.45 (208)	1.96 (238)	1.52 (244)	1.22 (174)
Peripheral arterial disease	3.81 (315)	2.72 (327)	1.94 (309)	1.70 (240)
All-cause death	24.25 (2100)	18.49 (2289)	13.72 (2231)	12.41 (1784)

Expressed as incidence rate per 100 person-years (no of events)

Figure Legends

Figure 1. Timeline for pivotal studies and guidelines on medical cardioprotective therapy in the study periods.
Footnote: Oxford Heart Protection Study[16], Stansby – Consensus Statement[17], Eurostar 2006[12], SVS (Society of Vascular Surgery) guidelines 2009[22], ESVS (European Society of Vascular Surgery) guidelines 2011[14], ESC (European Society of Cardiology) guidelines 2014[15], AAA - Abdominal Aortic Aneurysm.

Figure 2. Temporal changes in use of cardio-preventive therapy among patients with incident AAA according to history of atherosclerotic cardiovascular disease. A. Trends in use of antiplatelet, statin and recommended combined therapy with both drugs, B. Trends in antithrombotic therapy with either antiplatelets or OAC.

Figure 3. A. Cumulative incidence (with 95% CI intervals) of new atherosclerotic vascular admissions after AAA-diagnosis according to time periods. B. Cumulative mortality (with 95% CI intervals) according to time periods, overall and stratified on type of diagnosis (non-ruptured vs. ruptured).
Footnote: AAA -abdominal aortic aneurysm, CeVD – cerebrovascular disease, IHD – ischemic heart disease, PAD – peripheral arterial disease, MI – myocardial infarction

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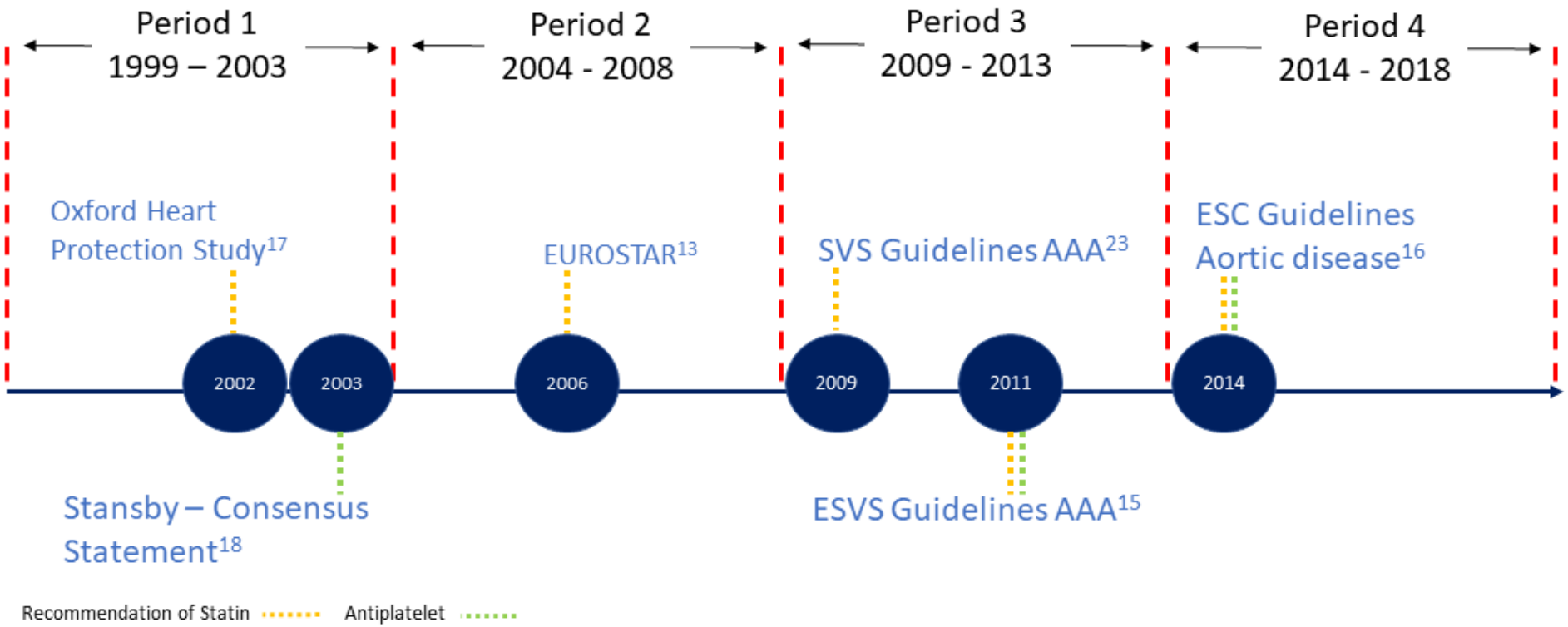

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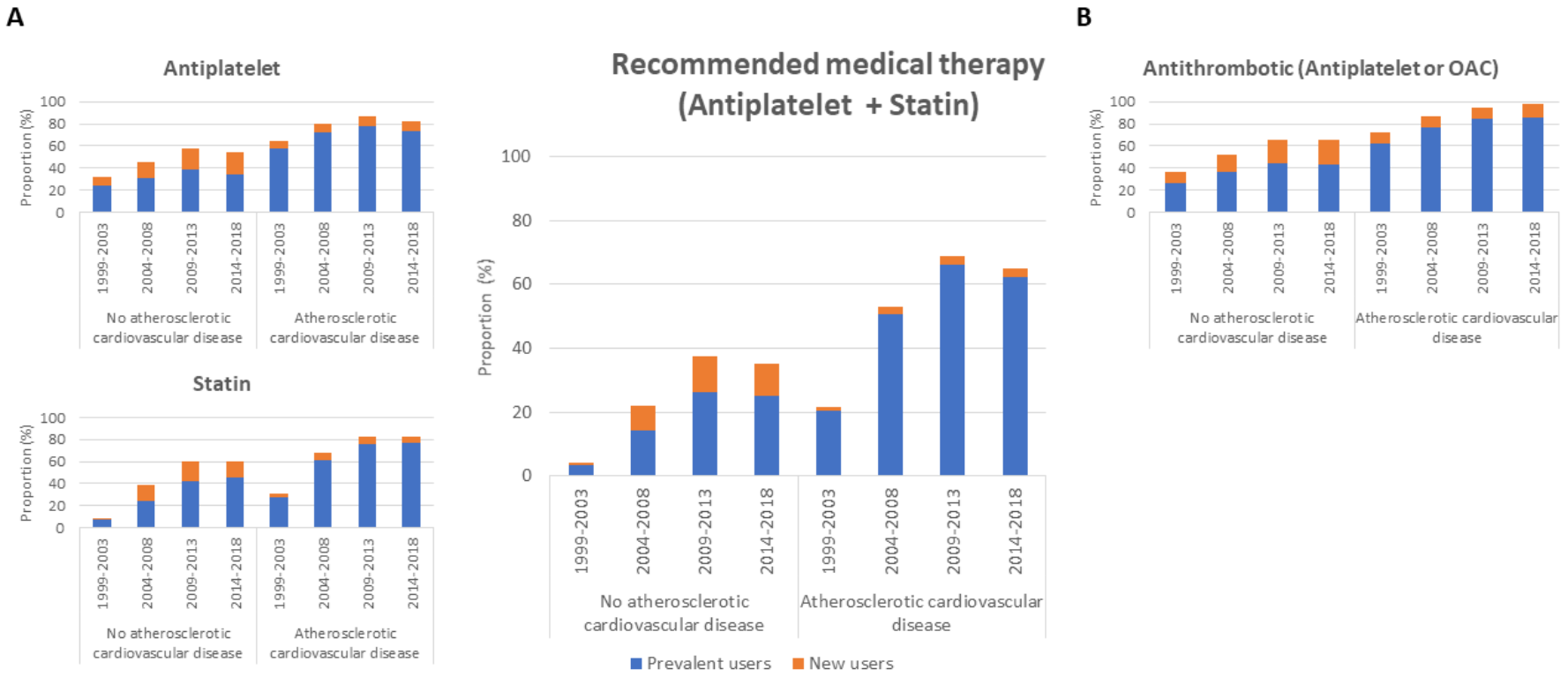

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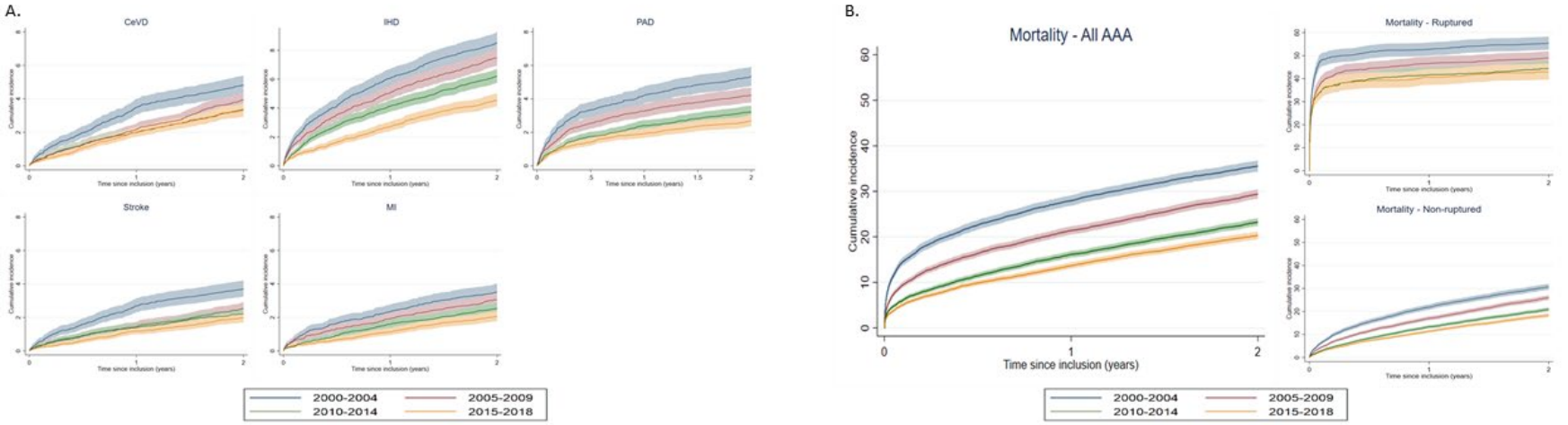

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