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Age- and Gender-related Differences in the Use of Secondary Medical Prevention after Primary Vascular Surgery: A Nationwide Follow-up Study

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WHAT THIS PAPER ADDS

- Compared to international guidelines the use of secondary medical prevention is insufficient among symptomatic peripheral artery disease (PAD) patients, but limited population-based data on the routine assessment of unselected patients exist. By coupling four Danish nationwide registers we aimed to clarify possible age and gender differences in-between 1996 and 2006.
- We found significant age differences in the late 1990s that appear to be substantially reduced in the first part of our follow-up period. Still the prescription rates in general were low compared with international guidelines. Continuous effort to ensure secondary medical prevention among symptomatic PAD patients regardless of age and gender is warranted.

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ABSTRACT

Objective: This study examined the possible age- and gender-related differences in the use of secondary medical prevention following primary vascular reconstruction in a population-based long-term follow-up study.
Methods: Using information from nationwide Danish registers, we identified all patients undergoing primary vascular reconstruction in-between 1996 and 2006 ($n = 20{,}761$). Data were obtained on all filled prescriptions 6 months and 3, 5 and 10 years after primary vascular reconstruction. Comparisons were made across age and gender groups, using men 40–60 years old as a reference.
Results: Compared to current guidelines the overall use of secondary medical prevention was moderate to low (e.g., lipid-lowering drugs 49.5%, angiotensin-converting enzyme inhibitors and angiotensin II receptor antagonists (ACE/ATII) 43.4%, combination of lipid-lowering drugs and anti-platelet therapy and any anti-hypertensive therapy 44.7%). A decline was observed between 6 months and 3 years after surgery. Patients >80 years old were less likely to be prescribed lipid-lowering drugs and combination therapy (e.g.: adjusted risk ratio (RR) 5 years after surgery for men and women 0.63 (95% confidence interval (CI): 0.39–1.02) and 0.48 (95%CI: 0.31–0.75), respectively, whereas smaller and statistical non-significant gender-related differences were observed. The age- and gender-related differences appeared eliminated or substantially reduced in the latest part of the study period (2001–2007).
Conclusion: We found moderate to low use of secondary medical prevention in Denmark compared with recommendations from clinical guidelines. However, the use has increased in recent years and age- and gender-related differences have been reduced or even eliminated.

Peripheral arterial disease (PAD) is a common manifestation of systemic atherosclerosis associated with significant morbidity and mortality (e.g., symptomatic PAD is associated with a 20–30% cumulative 5-year risk of non-fatal myocardial infarction and stroke).[1,2] The prevalence proportion of PAD increases dramatically with age (prevalence 15–20% in persons over 70 years old in developed countries) among both women and men and the number of PAD patients is therefore expected to increase substantially in the coming years due to the ongoing ageing of the population across most of the world.[3–6] PAD appears to progress

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more aggressively in women compared with men,[7,8] and women display more adverse symptoms at the time of diagnosis, faster functional decline and greater mobility loss.

Current national and international guidelines recommend lipid-lowering and anti-platelet therapy supplemented with anti-hypertensive treatment for all patients with symptomatic and asymptomatic PAD, independent of age and sex.[9–13] Several studies have indicated that the use of secondary medical prevention is generally insufficient for patients with PAD,[14–18] and there are data that suggest that under treatment, in particular affects women and the elderly.[8,19] However, important questions remain unanswered, as there are limited population-based data on the routine assessment of unselected patients.

We therefore aimed to determine whether there are age- and sex-related differences in the use of medical prophylaxis following primary vascular reconstruction for PAD in a population-based, nationwide study with a long-term follow-up and how these differences have responded to national and international efforts to ensure age- and gender-independent implementation of secondary medical prophylaxis to all PAD patients.

Materials and Methods

The entire Danish population ($n \approx 5.5$ million) is provided with tax-supported health care by the Danish National Health Service and is therefore allowed free access to hospital care, general practitioners and the reimbursement of expenses for a wide range of prescribed drugs. Each Danish citizen receives a unique civil registration number, which encodes gender and date of birth.

The civil registration number enables unambiguous individual linkage between population-based administrative and health-care registries. We established a data set for our study by electronically linking four nationwide medical registries on a patient level using the civil registration number of each patient.

Study population

The study population was identified in the Danish Vascular Registry and included all Danish patients with PAD undergoing primary vascular surgical as well as endovascular reconstruction between 1996 and 2007. The patients underwent surgery due to moderate intermittent claudication, ischaemic rest pain, ulceration or gangrene. The patients were only included with their first procedure during the study period. We excluded patients who died within 30 days after discharge and patients younger than 40 years, which resulted in a final total of 20,761 patients (Fig. 1).

The Danish Vascular Registry is a national clinical registry containing prospective information on all vascular procedures performed in Denmark since 1996. The primary objectives of the registry are surveillance and quality improvement, and it contains 65 variables, including indication for surgery, timing of surgery (acute/elective), patient characteristics, type of intervention, vascular patency at discharge, discharge destination and post-operative complications.[20] Reporting is mandatory for all vascular surgery departments ($n = 9$), and the registry covers 99.2% of all vascular procedures performed at Danish hospitals (www.karbase.dk, annual report 2009). To assess the data validity of the registry, we compared information recorded in the registry with information recorded in the medical records of 200 randomly selected patients. We found discrepancies in less than 1% for most variables, including vascular patency at discharge, and discrepancies in less than 3% for the type of surgery.

Information on the vital status of the patients during the follow-up period was obtained by linkage with the Danish Civil Registration System. This system has maintained electronic records of changes on the vital status of all citizens since 1968.[21]

Secondary medical prevention

Data on all prescriptions filled by the study population after discharge were obtained from the Medical Register of the Danish Medicines Agency. The registry contains data from 1995 onward for all prescriptions filled and dispensed at all Danish pharmacies, including the type of drug according to the Anatomical Therapeutical Chemical (ATC) classification system[22] and the date the drugs were dispensed. All cardiovascular drugs, except low-dose aspirin, require a prescription. However, regular aspirin is

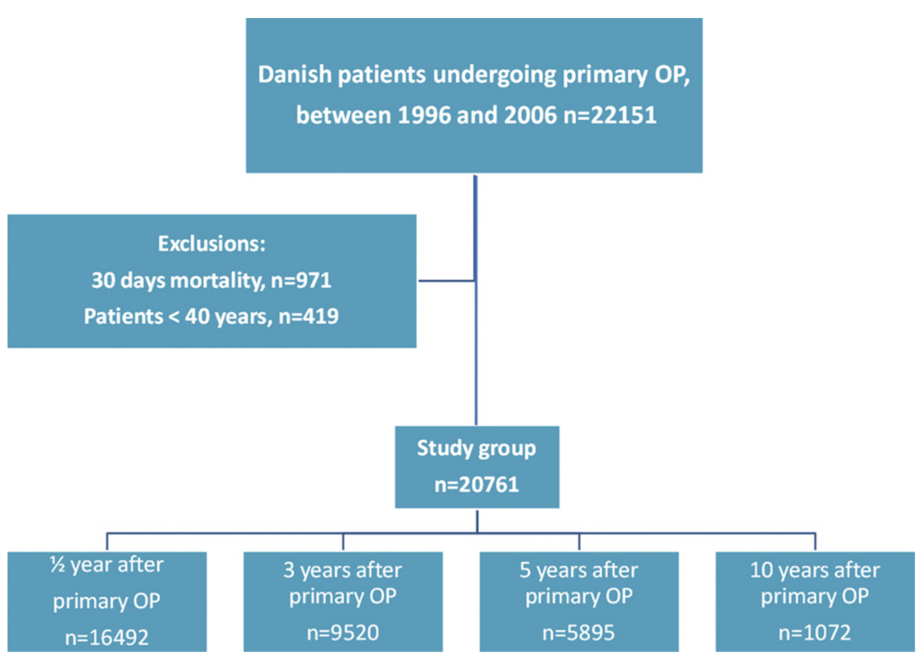

Figure 1. Flow diagram for the study population. Primary OP = Primary vascular surgical reconstruction.

available by prescription for patients with chronic diseases and to pensioners, and they are reimbursed for it. We identified all prescriptions filled by the patients up to 10 years after surgery, including prescription filled for anti-hypertensive drugs (angiotensin-converting enzyme inhibitors and angiotensin II receptor antagonists (ACE/ATII)), beta-adrenoceptor blocking agents (beta-blockers, calcium antagonists and diuretics), anti-platelet drugs (including low-dose aspirin, dipyridamole and clopidogrel) and lipid-lowering drugs.

Covariates

Data on covariates were obtained from the Danish National Patient Registry (co-morbidity), the Integrated Database for Labour Market Research (socioeconomic variables) and the Danish Vascular Registry. The Danish National Patient Registry retains information on all discharges from hospitals since 1977. The files include information on date of discharge for up to 20 discharge diagnoses and procedures, and they are coded according to the International Classification of Diseases (8th revision until 1993 and 10th revision thereafter).[23] We constructed the hospitalization history for all patients going back to 1977. Based on the history, we computed the co-morbidity index score (at the time of surgery) developed by Charlson et al.[24] The Charlson co-morbidity index covers 19 major disease categories (including myocardial infarction, heart failure, cerebrovascular diseases, diabetes and cancer) weighted according to their prognostic impact on patient survival. The index had previously been adapted and validated for use with hospital discharge registry data.[25] Three levels were defined: 'No co-morbidity' (score 0), 'low co-morbidity' (score 1–2), and 'high co-morbidity' (score >2).

The Integrated Database for Labour Market Research retains yearly updated information on socioeconomic status for the entire Danish population. We classified patients according to employment (employed, pensioner, or other), marital status (single, married, widowed, or divorced), gross income in quartiles and educational level (primary and lower secondary school, upper secondary school and vocational education and higher education).

The Danish Vascular Registry provided information on the following variables: acute/elective surgery, region of surgery (abdominal arteries (aorto-iliac), groin arteries and crural arteries), patency at discharge, discharge destination and smoking habits at the time of surgery.

Statistical analysis

All filled prescriptions were identified 6 months and 3, 5 and 10 years after primary vascular surgery reconstruction. The use of secondary medical prevention was defined as having filled at least one prescription within 90 days before or after each pre-defined time point. Patients who emigrated during the follow-up period were censored. Patient deaths during the follow-up period were recorded when they occurred. A generalised linear model based on the Poisson distribution in a log-linear model with robust error estimates was used to perform crude and adjusted comparisons across age and gender groups using men in the age category 40–60 years old as reference. We used this approach rather than a logistic regression because of the high prevalence of drug use and the need to adjust for a range of covariates, which may have caused convergence problems in a log-binomial model.[26,27]

In the adjusted analyses we included the co-morbidity index score and socioeconomic status (gross income, education level and

Table 1
Descriptive characteristics, stratified by sex and age.

Age/Sex	Female 40–60 years $N = 1906$ (9.2%)	Male 40–≤60 years $N = 3219$ (15.5%)	Female 60–≤80 years $N = 5930$ (28.6%)	Male 60–≤80 years $N = 7081$ (34.1%)	Female >80 years $N = 1586$ (7.6%)	Male >80 years $N = 1057$ (5.1%)
Comorb. Index						
None (0)	39.5	38.5	30.1	25.8	30.1	25.6
Low (1–2)	47.5	46.8	51.6	51.3	47.4	50.2
High (>2)	13.1	14.8	18.3	22.9	22.4	24.1
Operation type						
Abdominal arteries	66.0	51.9	45.8	39.9	19.7	26.1
Groin arteries	20.2	23.6	28.0	28.5	42.7	33.1
Crural arteries	13.9	24.3	26.2	32.1	37.6	40.8
Socioeconomic variables						
Marital status						
Married	62.6	57.8	42.1	64.6	14.7	52.2
Widow	7.6	2.8	39.2	14.8	73.2	39.0
Divorced	21.9	23.6	14.5	14.7	6.6	5.4
Un-married	7.8	15.8	4.3	6.0	5.6	3.4
Employment						
Employed	49.8	61.5	3.1	8.8	0.2	1.0
Pensioner	58.4	27.6	95.5	89.4	99.8	99.0
Other	11.9	10.9	1.4	1.8	0	0
Education level						
No information	0.1	2.0	6.9	6.0	68.3	61.9
primary and lower secondary school	59.2	9.6	65.2	45.2	23.9	18.7
Upper sec. school and vocational edu.	32.8	48.2	21.5	38.2	5.4	13.9
Higher education	7.3	10.1	6.9	10.6	2.4	6.0
Tobacco						
Non smoker	7.4	6.7	17.4	12.4	49.3	26.4
Formerly smoker	22.8	21.8	28.3	32.1	22.3	32.5
Current smoker	63.6	66.5	48.0	50.1	19.8	32.8
No information	6.2	5.3	6.3	5.3	8.7	8.2

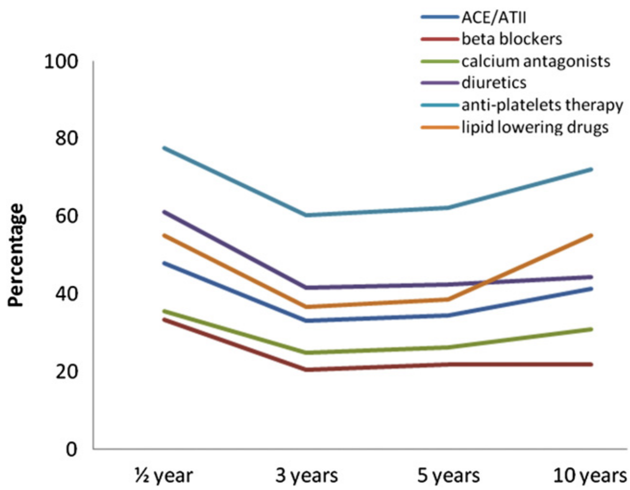

Figure 2. Percentage of patients filling prescriptions for secondary medical prevention 6 months 3, 5, and 10 years after primary vascular reconstruction.

marital status and employment) as covariates assessed 6 months and 3, 5 and 10 years after surgery as covariates. In addition, region of surgery (abdominal arteries (aorto-iliac), groin arteries and crural arteries), the timing of surgery (acute/elective), discharge destination, patency at discharge and smoking habits assessed at the time of surgery were also included. The number of patients who were >80 years old and available for a 10-year follow-up was too small to allow meaningful comparisons and these patients were therefore excluded from the multivariable analyses. Stratified analyses were according to calendar period (early (1996–2000) or late (2001–2007)). The year 2000 was used as the cutoff point because the first international guidelines for the management of PAD were published in that year.[28] Data were analysed using STATA version 11.0 (StataCorp.).

Results

Patients' characteristics

Descriptive characteristics of the study population are displayed in Table 1. The majority of the study population were 61 to ≤80 years old (63%) at the time of surgery. As expected, we found a higher level of co-morbidity among patients who were >80 years old compared to the younger age groups. A lower proportion of elderly patients underwent abdominal reconstruction, whereas no age- or gender-related differences were found for patency at discharge. More women than men lived alone in the two oldest age groups, and more women than men were discharged to their own homes among the patients who were >80 years old.

Overall use of secondary medical prevention

Fig. 2 shows the percentage of patients who filled prescriptions for secondary medical prevention at 6 months and 3, 5 and 10 years after the primary vascular reconstruction. A general decline (in the range of 10–20 percentage points) in drug use was seen between 6 months and 3 years after surgery. All examined drugs consistently appeared to follow this pattern. Thereafter, the level stabilised, with the exception of lipid-lowering drugs and anti-platelet drugs, which after 10 years had returned to the level observed after 6 months. The overall use of combination therapy (use of lipid-lowering + anti-platelet + any anti-hypertensive drugs) was modest (total mean of 44.7%). A total of 3.0% of the patients did not receive prescriptions for any form of secondary medical prevention during the follow-up period, and 75.9% of these patients were men (data not shown).

Age- and gender-related differences in use of secondary medical prevention

Fig. 3 shows the proportions of patients who received secondary medical prevention during the follow-up period, stratified by age

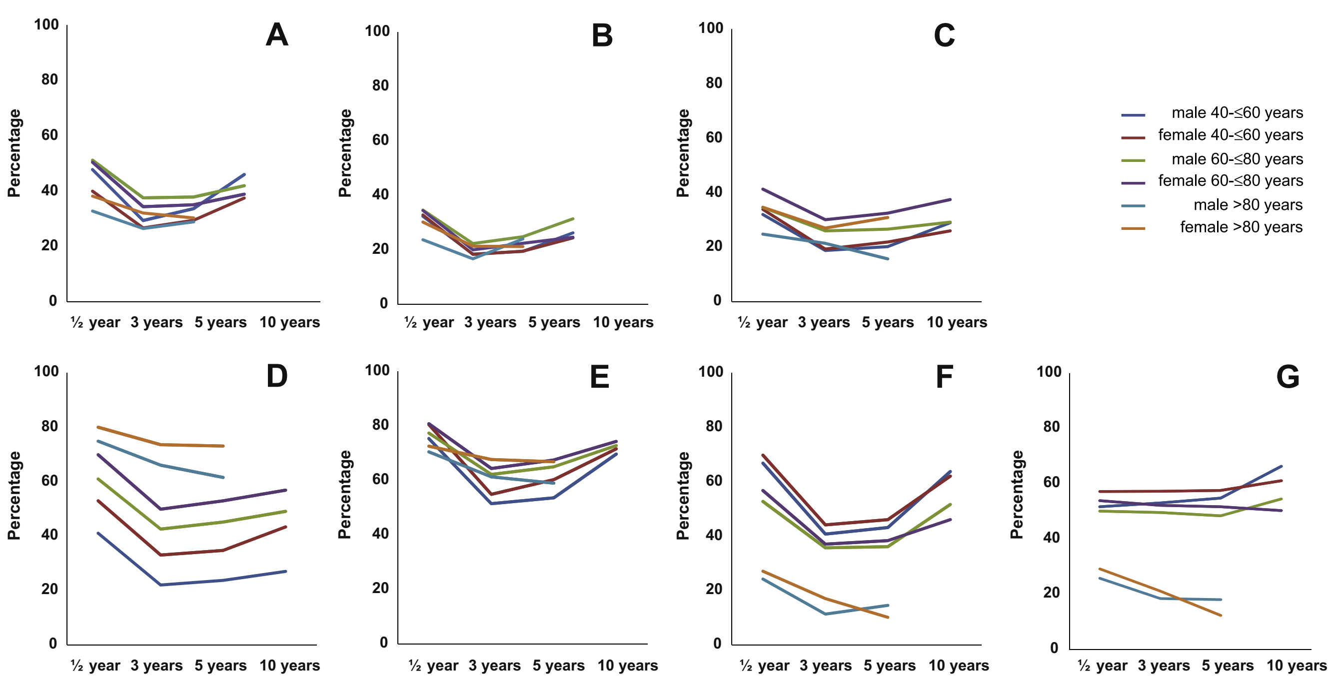

Figure 3. Percentage of patients filling prescriptions for secondary medical prevention 6 months, 3, 5, and 10 years after primary vascular reconstruction according to sex and age. A. ACE/ATII, B. Beta blockers, C. Calcium antagonists, D. Diuretics, E. Anti platelets therapy, F. Lipid lowering drugs, G. Combination therapy: lipid-lowering drugs, anti-platelets therapy, and any anti-hypertensive therapy.

and gender. Table 2 displays the corresponding adjusted relative risk (RR) estimates with 95% confidence intervals (95% CIs).

Patients who were >80 years old used lipid-lowering drugs and combination therapy less than younger patients (i.e., 25.8% and 29.2% of men and women who were >80 years old respectively, received combination therapy in the first 6 months following primary vascular reconstruction compared with 51.7% and 57.2%, respectively, among men and women who were 40–<60 years old). By contrast, elderly patients were more likely to receive diuretics, whereas no major age-related differences were observed for ACE inhibitors/ATII blockers, beta-blockers, calcium antagonists and anti-platelet drugs. However, the absolute age-related differences observed in Fig. 3 do not take into account the influence of possible confounding factors, including differences in co-morbidity and socioeconomic status. When adjusting for co-morbidity and socio-economic and clinical factors, we found no substantial age-related differences in the use of combination therapy in the first 6 months following primary vascular reconstruction (Table 2). However, age-related differences in the use of combination therapy persisted 3 and 5 years after surgery; men and women who were >80 years old had an adjusted RR (for receiving combination therapy) of 0.63 (95% CI: 0.39–1.02) and 0.48 (95% CI: 0.31–0.75) 5

Table 2
Adjusted relative risk (RR) for use of secondary medical prevention according to sex and age,6 months, 3, 5 and 10 years after primary vascular reconstruction.

	6 months Adjusted RR (95% CI) *N* = 16,492	3 years Adjusted RR (95% CI) *N* = 9520	5 years Adjusted RR (95% CI) *N* = 5895	10 years Adjusted RR (95% CI) *N* = 1072
ACE/ATII				
Females 40–≤60 years	0.87[0.81; 0.93]	0.92[0.81; 1.03]	0.86[0.76; 0.98]	0.80[0.65; 1.00]
Males 40–≤60 years	1	1	1	1
Females 60–≤80 years	1.05[0.99; 1.11]	1.13[1.02; 1.25]	0.96[0.85; 1.08]	0.77[0.61; 0.97]
Males 60–≤80 years	1.04[0.98; 1.10]	1.13[1.03; 1.24]	1.01[0.91; 1.12]	0.84[0.69; 1.103]
Females >80 years	0.99[0.89; 1.10]	1.55[1.28; 1.87]	1.15[0.85; 1.55]	
Males >80 years	0.81[0.72; 0.92]	1.20[0.94; 1.54]	1.07[0.72; 1.58]	
Beta-blockers				
Females 40–≤60 years	0.99[0.91; 1.08]	0.98[0.84; 1.15]	0.98[0.82; 1.18]	0.89[0.65; 1.20]
Males 40–≤60 years	1	1	1	1
Females 60–≤80 years	1.01[0.93; 1.10]	1.01[0.88; 1.17]	1.08[0.90; 1.27]	0.99[0.71; 1.36]
Males 60–≤80 years	0.98[0.91; 1.06]	1.02[0.89; 1.16]	1.12[0.96; 1.31]	1.19[0.89; 1.58]
Females >80 years	1.04[0.91; 1.20]	1.33[1.03; 1.47]	1.25[0.84; 1.84]	
Males >80 years	0.77[0.65; 0.91]	1.01[0.71; 1.42]	1.29[0.82; 2.05]	
Calcium antagonists				
Females 40–≤60 years	1.04[0.95; 1.13]	1.01[0.85; 1.16]	1.07[0.90; 1.28]	0.87[0.65; 1.17]
Males 40–≤60 years	1	1	1	1
Females 60-≤80 years	1.18[1.09; 1.28]	1.41[1.23; 1.61]	1.46[1.24; 1.69]	1.11[0.83; 1.49]
Males 60–≤80 years	1.00[0.92; 1.08]	1.19[1.04; 1.36]	1.19[1.02; 1.38]	0.90[0.68; 1.19]
Females >80 years	1.04[0.92; 1.19]	1.26[1.00; 1.59]	1.48[1.08; 2.03]	
Males >80 years	0.73[0.62; 0.86]	0.97[0.72; 1.30]	0.75[0.44; 1.30]	
Diuretics				
Females 40–≤60 years	1.21[1.14; 1.30]	1.42[1.26; 1.60]	1.38[1.21; 1.58]	1.50[1.18; 1.92]
Males 40–≤60 years	1	1	1	1
Females 60–≤80 years	1.36[1.27; 1.43]	1.75[1.58; 1.95]	1.69[1.50; 1.92]	2.62[1.28; 2.05]
Males 60–≤80 years	1.23[1.16; 1.30]	1.53[1.37; 1.69]	1.52[1.34; 1.71]	1.47[1.17; 1.86]
Females >80 years	1.34[1.25; 1.44]	2.24[1.96; 2.57]	2.06[1.73; 2.45]	
Males >80 years	1.28[1.19; 1.38]	2.03[1.74; 2.36]	1.83[1.46; 2.30]	
Anti-platelet therapy				
Females 40–≤60 years	1.06[1.02; 1.09]	1.06[0.99; 1.31]	1.09[1.01; 1.18]	1.00[0.89; 1.12]
Males 40–≤60 years	1	1	1	1
Females 60–≤80 years	1.06[1.02; 1.10]	1.16[1.09; 1.24]	1.16[1.08; 1.24]	1.06[0.94; 1.19]
Males 60–≤80 years	1.02[0.99; 1.05]	1.11[1.05; 1.18]	1.12[1.04; 1.20]	1.02[0.91; 1.14]
Females >80 years	1.01[0.95; 1.06]	1.34[1.20; 1.49]	1.25[1.07; 1.45]	
Males >80 years	0.97[0.91; 1.03]	1.20[1.05; 1.36]	1.09[0.89; 1.34]	
Lipid-lowering drugs				
Females 40–≤60 years	1.09[1.04; 1.13]	1.19[1.09; 1.29]	1.10[0.99; 1.21]	1.02[0.88; 1.18]
Males 40–≤60 years	1	1	1	1
Females 60–≤80 years	1.04[0.99; 1.09]	1.21[1.10; 1.31]	1.03[0.93; 1.14]	0.88[0.74; 1.05]
Males 60–≤80 years	0.88[0.84; 0.92]	0.98[0.90; 1.07]	0.86[0.78; 0.95]	0.87[0.75; 1.02]
Females >80 years	1.03[0.92; 1.14]	1.49[1.17; 1.89]	0.83[0.49; 1.40]	
Males >80 years	0.81[0.71; 0.92]	0.89[0.62; 1.28]	0.96[0.53; 1.72]	
Combination therapy[a]				
Females 40–≤60 years	1.12[1.06; 1.19]	1.11[1.03; 1.18]	1.06[0.98; 1.15]	0.94[0.82; 1.08]
Males 40–≤60 years	1	1	1	1
Females 60–≤80 years	1.16[1.10; 1.22]	1.10[1.03; 1.18]	1.01[0.93; 1.09]	0.83[0.71; 0.98]
Males 60–≤80 years	1.00[0.95; 1.05]	0.96[0.90; 1.02]	0.87[0.80; 0.94]	0.83[0.72; 0.96]
Females >80 years	1.23[1.11; 1.37]	0.93[0.76; 1.15]	0.48[0.31; 0.75]	
Males >80 years	0.98[0.86; 1.12]	0.75[0.57; 1.00]	0.63[0.39; 1.02]	

Adjusted for age, Charlson's co-morbidity index, socioeconomic status (gross income, education level, marital status and employment), smoking, acute/non-acute surgery, discharge destination and patency at discharges.

[a] Combination therapy: Lipid-lowering drugs, anti-platelets therapy, and any anti-hypertensive therapy.

years after surgery, respectively, compared with men who were 40 to ≤60 years old. No other major age-related differences in the use of secondary medical prevention were identified in the multivariable analyses.

More women than men in general appeared to receive secondary medical prevention (in particular diuretics, anti-platelet therapy and calcium antagonists) although it is important to notice that many of the observed gender-related differences did not reach statistical significance (Table 2). When we stratified the analyses into early (1996–2000) and late (2001–2007) periods, and focused on prescriptions filled 6 months after surgery, we found striking differences regarding the use of secondary medical prevention (Table 3 and Fig. 4). In the early period, substantial age-related differences were observed for several drugs, particularly lipid-lowering and combination therapies. Thus, the adjusted RRs of combination therapy were as low as 0.19 (95% CI: 0.09–0.38) and 0.27 (95% CI: 0.16–0.46) among men and women who were >80 years old, respectively, compared with men who were 40 to ≤60 years old in the early period. These age-related differences for all drugs were either completely eliminated or substantially reduced in size during the late period.

Table 3
Adjusted relative risk (RR) for prescription of secondary medical prevention according to sex and age 6 months after primary vascular reconstruction according to hospitalization period: Early (1996–2000) or late (2001–2007).

	Early period 1996–2000 Adjusted RR	Late period 2001–2007 Adjusted RR
ACE/ATII		
Males 40–≤60 years	1	1
Males 60–≤80 years	1.04[0.98; 1.10]	1.06[0.98; 1.14]
Males > 80 years	0.81[0.72; 0.92]	0.82[0.71; 0.96]
Females 40–≤60 years	0.89[0.80; 0.98]	0.85[0.77; 0.93]
Females 60–≤80 years	0.99[0.90; 1.08]	1.02[0.94; 1.11]
Females >80 years	0.87[0.71; 1.06]	0.86[0.76; 0.99]
Beta-blockers		
Males 40–≤60 years	1	1
Males 60–≤80 years	0.90[0.80; 1.01]	0.97[0.87; 1.08]
Males >80 years	0.58[0.42; 0.79]	0.72[0.59; 0.88]
Females 40–≤60 years	0.96[0.84; 1.09]	0.99[0.88; 1.12]
Females 60–≤80 years	0.99[0.87; 1.12]	0.92[0.82; 1.12]
Females > 80 years	0.79[0.62; 1.02]	0.90[0.76; 1.07]
Calcium antagonists		
Males 40–≤60 years	1	1
Males 60–≤80 years	0.89[0.80; 0.99]	1.08[0.96; 1.20]
Males >80 years	0.61[0.47; 0.80]	0.85[0.69; 1.04]
Females 40–≤60 years	1.04[0.92; 1.17]	1.03[0.91; 1.17]
Females 60–≤80 years	1.15[1.03; 1.29]	1.20[1.07; 1.35]
Females >80 years	0.89[0.72; 1.09]	1.18[0.99; 1.41]
Diuretics		
Males 40–≤60 years	1	1
Males 60–≤80 years	1.20[1.12; 1.30]	1.26[1.15; 1.37]
Males >80 years	1.27[1.15; 1.41]	1.39[1.24; 1.55]
Females 40–≤60 years	1.23[1.13; 1.33]	1.21[1.10; 1.33]
Females 60–≤80 years	1.33[1.24; 1.44]	1.37[1.25; 1.49]
Females >80 years	1.32[1.20; 1.45]	1.41[1.27; 1.57]
Anti-platelet therapy		
Males 40–≤60 years	1	1
Males 60–≤80 years	1.00[0.95; 1.05]	1.02[0.98; 1.07]
Males >80 years	0.91[0.82; 1.02]	0.97[0.90; 1.05]
Females 40–≤60 years	1.07[1.02; 1.13]	1.05[1.00; 1.09]
Females 60–≤80 years	1.06[1.01; 1.12]	1.05[1.01; 1.09]
Females >80 years	0.98[0.89; 1.07]	0.99[0.92; 1.06]
Lipid-lowering drugs		
Males 40–≤60 years	1	1
Males 60–≤80 years	0.68[0.62; 0.75]	0.93[0.89; 0.98]
Males > 80 years	0.20[0.10; 0.40]	0.71[0.62; 0.81]
Females 40–≤60 years	1.07[0.99; 1.16]	1.06[1.01; 1.12]
Females 60–≤80 years	0.86[0.78; 0.95]	1.04[0.99; 1.09]
Females >80 years	0.33[0.21; 0.53]	0.85[0.76; 0.94]
Combination therapy[a]		
Males 40–≤60 years	1	1
Males 60–≤80 years	0.71[0.64; 0.79]	1.09[1.02; 1.15]
Males >80 years	0.19[0.09; 0.38]	0.86[0.75; 0.98]
Females 40–≤60 years	1.09[0.99; 1.20]	1.11[1.04; 1.19]
Females 60–≤80 years	0.90[0.80; 1.00]	1.18[1.10; 1.25]
Females > 80 years	0.27[0.16; 0.46]	1.01[0.91; 1.13]

Adjusted for age, Charlson's co-morbidity index, socioeconomic status (gross income, education level, marital status and employment), smoking, acute/non-acute surgery, discharge destination and patency at discharges.

[a] Combination therapy: Lipid-lowering drugs, anti-platelets therapy, and any anti-hypertensive drug therapy.

Discussion

We found moderate to low use of secondary medical prevention following primary vascular reconstruction in Denmark between 1996 and 2007 compared with national and international guidelines recommendations.[10–13] Substantial age-related and, to some extent, gender-related differences were observed in the late 1990s; however, these differences appear to have been eliminated or substantially reduced in recent years.

The vascular surgical activity in Denmark appear to be comparable to Western countries with 14.4/100,000 inhabitants per year receiving infrainguinal bypass compared with a range of 2.3–24.6/100,000 inhabitants per year in other Western countries with vascular registries (according to the Vascunet committee under ESVS, numbers provided by Dr. Leif Panduro Jensen). The low use of secondary medical prophylaxis found in our study is not only in accordance with previous smaller Danish studies[16,29,30] but also consistent with findings from other populations, as reported in a recent systematic review on the implementation of established recommended secondary medical prevention in patients with symptomatic PAD, including 24 observational studies containing 34,157 patients.[15]

Age- and gender-related differences

We found persistent age- and gender-related differences in the use of secondary medical prevention in the overall analyses, even after adjusting for socio-demographic and clinical factors. The gap between the crude and adjusted RRs indicates that the differences in drug use were at least partly explained by confounding by socio-demographic and clinical factors. Ignoring these factors would have caused us to overestimate the true size of the age- and gender-related differences in drug use. No previous studies have, to our knowledge, explored the possible existence and size of age-related differences in the use of secondary medial prevention among PAD patients. However, age-related differences in the use of secondary medical prevention have previously been found among patients with ischaemic stroke[31–33] and acute coronary syndrome,[34] which indicate that age-related differences in the use of secondary medical prevention are a widespread phenomenon among patients with cardiovascular disease. Gender-related differences in the use of secondary medical prevention have previously been reported among PAD patients;[8] men showed a higher chance of receiving lipid-lowering therapy (adjusted odds ratio (OR) = 1.3), anti-platelet therapy (OR = 1.6) and ACE/ATII and beta-blockers (OR = 1.4) compared with women. However, in contrast to these findings, women generally appeared to have the highest chance of receiving secondary medical prevention in our study although the differences in general were modest and often did not reach statistical significance. The inconsistency of the studies may possibly reflect differences in the median age and stages of PAD in the study populations.

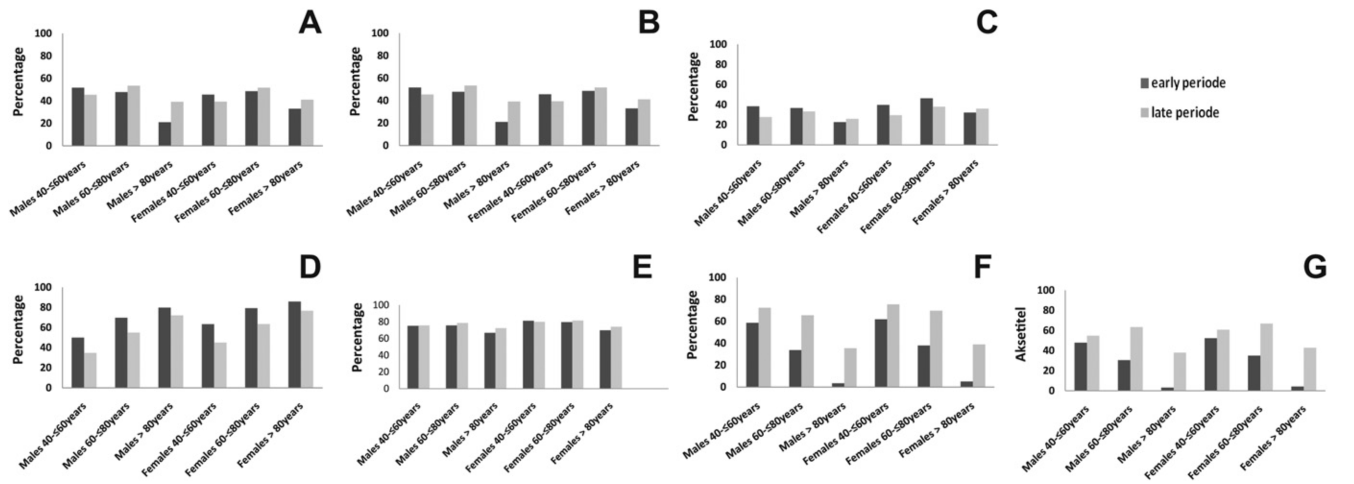

Figure 4. Percentage of patients filling prescriptions for secondary medical prevention after primary vascular reconstruction according to hospitalization period: Early (1996–2000) or late (2001–2007). A. ACE/ATII, B. Beta blockers, C. Calcium antagonists, D. Diuretics, E. Anti platelets therapy, F. Lipid lowering drugs, G. Combination therapy: lipid-lowering drugs, anti-platelets therapy, and any anti-hypertensive therapy.

Stratifying our study period into early (1996–2000) and late (2001–2007) periods revealed that the age- and gender-related differences in the use of secondary medical prevention have disappeared or at least substantially decreased in recent years. This positive development parallels the publication of international and national clinical guidelines recommending the routine use of secondary medical prevention to all PAD patients independent of age and gender.[10–13]

Strengths and limitations of this study

The major strengths of our study include the population-based design, availability of detailed individual-level data and complete follow-up. The validity of our estimates depends on the accuracy of the used data sources. The accuracy of The Danish Vascular Registry was previously described as good.[20] Our study confirms this accuracy, as we found good agreement when comparing data from the Danish Vascular Registry with information from the patients' medical records. From the Danish Patient Registry, we obtained data on the co-morbidities of the patients. The predictive value has also previously been reported to be high for a range of important diagnoses in the Danish Patient Registry, including myocardial infarction, cancer and diabetes.[35] However, despite controlling for a wide range of covariates, we cannot entirely exclude the possibility of residual or unaccounted confounding, for example, the Charlson co-morbidity index does not reflect the severity of the individual co-morbidities, and other factors not included in our analyses (including industry-sponsored campaigns, preferences of general practitioners, etc.) may also potentially have influenced the use of secondary medical prophylaxis. Furthermore, we used filled prescriptions as a proxy for actual drug use. We could therefore not be certain that the patients actually did take the drugs; although the fact that the patients paid a part of the cost of the drugs out of their own pocket do indicate that a filled prescription is likely to reflect actual drug use. From the available data, it was not possible to determine whether a lack of drug use indicated that a drug had not been prescribed by a physician or that the patient did not fill the prescription at a pharmacy.

Conclusion

We found insufficient use of secondary medical prevention among Danish patients undergoing primary vascular reconstruction between 1996 and 2007 compared with national and international clinical guidelines. Substantial age-related, and to some extent, also gender-related differences were observed in the late 1990s; however, these differences appear to have been eliminated or substantially reduced in recent years. Continuous efforts are warranted to ensure optimal secondary medical prevention among PAD patients who undergo primary vascular reconstruction, regardless of age and gender.

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Conflict of Interest

None.

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