Taylor & Francis Taylor & Francis Group

RESEARCH ARTICLE

Drug prescription rates in secondary cardiovascular prevention in old age: Do vulnerability and severity of the history of cardiovascular disease matter?

Petra G. van Peet, Jacobijn Gussekloo, Wendy P.J. den Elzen, Jeanet W. Blom, Margot W.M. de Waal, and Wouter de Ruijter

Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, The Netherlands

ABSTRACT

Objective: To assess the influence vulnerability and severity of cardiovascular disease (CVD), on prescription rates of secondary cardiovascular preventive drugs in old age.

Design: Population-based observational study within the ISCOPE study.

Setting: General practices in the Netherlands.

Subjects: A total of 1350 patients with a history of CVD (median age 81 years, 50% female). Main outcome measures. One-year prescription rates of lipid-lowering drugs and antithrombotics were obtained from the electronic medical records of 46 general practitioners (GPs). Prescription of both drugs for ≥ 270 days per year was considered optimal. GPs made a judgement of vulnerability. Severity of CVD was expressed as major (myocardial infarction, stroke, or arterial surgery) versus minor (angina, transient ischaemic attack, or claudication).

Results: GPs considered 411 (30%) participants to be vulnerable and 619 (55%) participants had major CVD. Optimal treatment was prescribed to 680 (50%) participants, whereas 370 (27%) received an antithrombotic drug only, 53 (4%) a lipid-lowering drug only, and 247 (18%) received neither. Optimal treatment was lower in participants aged \geq 85 years (OR 0.37 [95% CI 0.29–0.48]), in females (OR 0.63 [0.50–0.78]), in vulnerable persons (OR 0.79 [0.62–0.99]) and in participants with minor CVD (OR 0.65 [0.53–0.81]). Multivariate ORs remained similar whereas vulnerability lost its significance (OR 0.88 [0.69–1.1]).

Conclusion: In old age, GPs' judgement of vulnerability is not independently associated with lower treatment rates of both lipid-lowering drugs and antithrombotics, whereas a history of minor CVD is. Individual proactive re-evaluation of preventive treatment in older (female) patients, especially those with a history of minor CVD, is recommended.

KEY POINTS

- Prescriptions of lipid-lowering drugs and antithrombotics in secondary cardiovascular prevention tend to decline with age.
- In this study with median age 81 years, 50% of participants received optimal treatment with both lipid-lowering drugs and antithrombotics.
- GPs' judgement of vulnerability was not independently associated with optimal treatment.
- A history of less severe cardiovascular disease was independently associated with lower prescription rates of lipid-lowering drugs and antithrombotics.
- Proactive individual re-evaluation of cardiovascular preventive treatment in older (female) patients, especially patients with less severe cardiovascular disease, is recommended.

ABBREVIATIONS: ATC: Anatomical Therapeutic Chemical; CABG: coronary artery bypass grafting; CI: confidence interval; CVD: cardiovascular disease; EMR: electronic medical records; ICPC: International Classification of Primary Care; ISCOPE: Integrated Systematic Care for Older Persons; MI: myocardial infarction; GP: general practitioner; OR: odds ratio; PAD: peripheral arterial disease; PTCA: percutaneous coronary intervention; TIA: transient ischaemic attack

ARTICLE HISTORY

Received 18 November 2014 Accepted 2 October 2015

KEYWORDS

Cardiovascular diseases; drug prescriptions; general practice; old age; secondary prevention; the Netherlands; vulnerability

Introduction

In ageing societies cardiovascular disease (CVD) is an important cause of disability and mortality [1,2]. Secondary preventive treatment is effective up to a

high age [3–8], and lifelong lipid-lowering drugs and antithrombotics are recommended in all guidelines for secondary prevention [9–12]. However, although prescription of preventive treatment has generally increased

CONTACT Petra G van Peet P.G.van_Peet@lumc.nl Department of Public Health and Primary Care, Leiden University Medical Center, PO Box 9600, 2300 RC Leiden, The Netherlands

Supplemental data for this article can be accessed http://dx.doi.org/10.3109/02813432.2015.1117281.

in the last decades, treatment in older age groups still lags behind [13-16].

Decreasing life expectancy, in combination with the lag time to benefit [17], may influence physicians and older persons when deciding not to start or to stop secondary cardiovascular preventive treatment in old age. The START criteria do not recommend starting of statin therapy in patients aged 85 years and over, because of lack of evidence based on randomised controlled trials (RCTs) in this age group. However, the STOPP criteria do not advise stopping these medications in very old age [18]. In (very) old age, medical care is often more personalised, taking into account all comorbidities and individual patient preferences. The eventual prescription of secondary cardiovascular preventive treatment is the result of this complex interaction between physician and patient.

As the general practitioner's (GP's) judgement of vulnerability may affect treatment decisions [19], more data on the influence of vulnerability on the intensity of secondary cardiovascular preventive medication is required [20]. In general, vulnerable patients might receive fewer preventive drugs than fit older people [21,22], although, ultimately, vulnerability should not be viewed as a reason to withhold care, but rather as a means of delivering it in a more patient-centred fashion [23] For secondary cardiovascular preventive medication this topic is not well studied.

Medical history can influence a GP's judgement of vulnerability, but has also been related to prescription rates themselves: a history of less severe CVD, such as angina, transient ischaemic attack, or claudication, as opposed to myocardial infarction, stroke, or arterial surgery, can be associated with reduced prescription rates [24,25].

It is unknown whether GPs' judgement of vulnerability, or the severity of the CVD history, might (in part) explain the observed low prescription rates of secondary cardiovascular preventive medication in (very) old age.

We hypothesised that vulnerability and less severe CVD might be associated with lower prescription rates of cardiovascular preventive drugs in old age, and investigated the associations of prescription rates of lipidlowering drugs and antithrombotics with age, sex, GPs' judgement of vulnerability and the severity of CVD, in a population-based sample of participants aged > 75 years with a history of CVD.

Material and methods

The present study is embedded in the ISCOPE (Integrated Systematic Care for Older Persons) study. The ISCOPE study is a cluster randomised trial among persons aged \geq 75 years from 59 general practices in and around the city of Leiden (the Netherlands), who were invited to participate (inclusion period September 2009 to September 2010) [26]. The aim was to evaluate the effectiveness of a tailored care plan carried out by the GP for older persons with complex health problems, using a functional approach for older people.

Informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. The Medical Ethics Committee of the Leiden University Medical Centre approved the study. The study is registered in the Netherlands Trial Register (Registration number: 1946).

Cardiovascular disease history

The history of cardiovascular disease in the electronic medical records (EMR) was defined by the presence of International Classification of Primary Care (ICPC) codes K74, K75, K76, K89, K92 (excluded K92.2 and K92.3 and text words M. Raynaud and M. Buerger), and K99.01, or an episode with the text words angina, myocardial infarction (MI), ischaemic heart disease, transient ischaemic attack (TIA), stroke (intermittent claudication), peripheral arterial disease (PAD), or aneurysm, respectively. An episode with text words coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PTCA) or surgery for peripheral arterial disease was coded as surgery for arterial disease.

Medication use

The Anatomical Therapeutic Chemical (ATC) code C10 was used to select lipid-lowering drugs, and ATC codes B01AA (anticoagulants) and B01AC (antiplatelet drugs) to select antithrombotics. All participants with prescriptions for > 270 days during the year after study entrance were considered current users of this type of drug. Optimal treatment was defined as the prescription of both a lipid-lowering drug and an antithrombotic drug; suboptimal treatment was defined as the current prescription of only one of these two types of drugs; and poor treatment was defined as the current use of neither.

Additional parameters

Age. Participants were divided into two age groups: those aged 75–84 years (old age) and those aged \geq 85 years (very old age).

GPs' judgement of vulnerability. Before inviting the older people to participate, we asked GPs to classify all enlisted older people into three categories according to

their own perception: (i) not vulnerable, (ii) possibly vulnerable, and (iii) vulnerable. To include only those participants that were with certainty considered to be vulnerable in the vulnerable group, we combined the 'not vulnerable' or 'possibly vulnerable' participants and compared them with the vulnerable participants.

Severity of cardiovascular disease history. The participants were classified according to the severity of their CVD history. Minor CVD included angina, transient ischaemic attack, or peripheral arterial disease without surgery, whereas major CVD included myocardial infarction, stroke, or surgery for arterial disease. In addition, we created groups according to the number and type of cardiovascular beds involved: cardiac bed (angina, MI or ischaemic heart disease), cerebral bed (TIA or stroke), and peripheral artery bed (intermittent claudication or aneurysm).

Statistical analysis

Categorical variables were expressed in percentages. Differences between groups in categorical variables were analysed using Pearson's chi-square test.

Associations between the percentage of prescriptions (prescription rates) and age groups, sex, GPs' judgement of vulnerability, and severity of CVD were investigated with logistic regression models. Univariate and multivariate odds ratios (OR) with 95% confidence intervals (CIs) were estimated for the relation between these variables and prescription rates; a possible interaction between age and the other variables was also tested. No additional adjustments were made for depressive symptoms, cognition, functional status, and other comorbidities, because these latter characteristics are included in the GPs' judgement of vulnerability.

For additional analyses regarding age, we calculated ORs with dichotomisation on the median age and for tertiles of age. With regard to vulnerability, all analyses were repeated with the exclusion of the 'possibly vulnerable' participants. Concerning the severity of CVD status, prescription rates were calculated for participants with only one cardiovascular bed involved, and for participants with more than one cardiovascular bed involved.

For sensitivity analysis, prescription rates were also calculated stratified for participants with a cardiovascular disease within two years before the start of the ISCOPE study, and participants with an event longer ago.

Data analyses were performed using SPSS 20 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Of the 11 476 eligible persons, 7285 (63%) from 59 general practices participated in the screening phase of the study (additional online file: Flow chart of participants in the study). After one year, complete electronic medical records (EMR) were available for 4361 (38%) participants (EMR of participants who gave consent and were not lost to follow up, from the 46 general practices with an EMR compatible with extraction of data for our research question). Of these 4361 participants, 1350 participants (33%) had a history of CVD, according to their EMR. Complete data on drug prescriptions from the EMRs were available from study entrance until one-year follow-up for all these 1350 participants.

Baseline characteristics

The median age of the 1350 participants with a history of CVD in the ISCOPE study was 81 years (interquartile range 78–85 years, age range 75–101 years), 26% were aged \geq 85 years, and 50% were female (Table 1). GPs considered 411 (30%) participants to be vulnerable. Minor CVD was present in 619 (46%) of the participants.

Current prescription of lipid-lowering drugs was seen in 54% of the participants, and current prescription of antithrombotics in 78%. Optimal prescription of both drugs was seen in 50% of the participants. Suboptimal treatment was seen in 31%: 27% used an antithrombotic drug only and 4% a lipid-lowering drug only. Poor treatment was observed in 18% of the participants.

Determinants of prescription rates

Table 2 and Figure 1 present the optimal prescription rates of lipid-lowering drugs and antithrombotics according to age, sex, GPs' judgement of vulnerability, and severity of the CVD history. Participants aged \geq 85 years, females, vulnerable participants, and participants with minor CVD all had lower optimal prescription rates (33%, 45%, 46%, and 45%, respectively) compared with participants aged 75–84 years, males, non-vulnerable participants or participants with major CVD (57% [p<0.01], 56% [p<0.01], 52% [p<0.05], and 55% [p<0.01], respectively).

In contrast, prescription of antithrombotics only (no lipid-lowering drugs) was more often observed in participants aged \geq 85 years, in females, and in vulnerable participants. In the age group \geq 85 years, about 25% were receiving neither of the two drugs.



Table 1. Sociodemographics and clinical characteristics of participants with a history of cardiovascular disease from the ISCOPE study (n = 1350).

	n (%)
Sociodemographic	
Age in years (median (interquartile range))	81 (78–85)
Male	678 (50)
GPs' judgement of vulnerability ¹	
Vulnerable	411 (30)
Possibly or not vulnerable	927 (69)
Cardiovascular disease history ²	
Severity	
Minor cardiovascular disease ³	619 (46)
Major cardiovascular disease ⁴	731 (54)
Type of vascular bed	
Cardiac	834 (62)
Angina	428 (32)
Myocardial infarction	377 (28)
Ischaemic heart disease	122 (9)
Cerebral	494 (37)
Transient ischaemic attack	246 (18)
Stroke	257 (19)
Peripheral	253 (19)
Intermittent claudication	195 (14)
Aneurysm	68 (5)
Cardiovascular preventive treatment with lipid-lowering or antithrombotic drugs	
Type	
Lipid-lowering drug⁵	733 (54)
Antithrombotic drugs (aspirin or oral anticoagulant)	1050 (78)
Completeness of treatment	
Optimal treatment: both lipid-lowering drug and antithrombotic drug ⁶	680 (50)
Suboptimal treatment: lipid-lowering drug only	53 (4)
Suboptimal treatment: anti-thrombotic drug only	370 (27)
Poor treatment: no lipid-lowering or antithrombotic drug	247 (18)

¹Assessed before screening (12 missing values); vulnerable participants versus possibly vulnerable (n = 360), not vulnerable (n = 513), or don't know (n = 54); ²obtained from EMR general practitioners; ³history of angina, transient ischaemic attack, or intermittent claudication; ⁴history of myocardial infarction, stroke, or arterial surgery; ⁵use of statins (n = 1336) or other lipid-lowering drugs (n = 14); ⁶use of both drugs for more than 270 days during the first year of the ISCOPE study.

Table 2. Prescription rates (%) of lipid-lowering and/or antithrombotic drugs¹ in participants with a history of cardiovascular disease from the ISCOPE study (n = 1350).

	Age		Sex		Vulnerability ²		CVD history ³	
	≥ 85 ($n = 347$)	75–84 (<i>n</i> = 1003)	female (<i>n</i> = 678)	male (n = 672)	yes (n = 411)	no (n = 927)	minor (n = 619)	major (n = 731)
Optimal treatment (both drugs) Suboptimal treatment	33	57 ⁴	45	56 ⁴	46	52 ⁵	45	55 ⁴
antithrombotic drug only lipid-lowering drug only	40 2	23 ⁴ 5	32 5	23 ⁴ 3	30 3	26 ⁵ 4	29 5	26 3
Poor treatment (none of the two)	25	16 ⁴	19	18	21	17	21	16 ⁵

CVD: cardiovascular disease. 1 More than 270 days prescription of lipid-lowering and/or antithrombotic drugs in the year after start of ISCOPE study; 2 assessed before screening (12 missing values); vulnerable ('yes') versus possibly vulnerable, not vulnerable participants, or do not know (together 'no'); ³minor CVD: history of angina, transient ischaemic attack, and/or claudication; major CVD: history of myocardial infarction, stroke, and/or arterial surgery; 4Pearson's chisquare p < 0.01 (as compared with > 85 years, female, vulnerable or minor CVD, respectively); ⁵Pearson's chi-square p < 0.05 (as compared with vulnerable, and as compared with minor CVD, respectively).

Table 3 presents univariate and multivariate ORs for age > 85 years, female sex, minor CVD, and GPs' judgement of vulnerability, with regard to the prescription of both drugs. Age was the strongest predictor (OR for age \geq 85 years 0.37 [0.29–0.48]), followed by female sex (0.63 [0.50-0.78]), minor CVD (0.65 [0.53-0.81]), and GPs' judgement of vulnerability (0.79 [0.62-0.99]). In the multivariate analyses, associations remained similar,

although GPs' judgement of vulnerability lost its significance (multivariate OR 0.88 [0.69-1.1]). There was no interaction between age and the other three variables (data not shown).

Additional analyses

For additional analyses with regard to age, we dichotomised the participants into two groups according to the

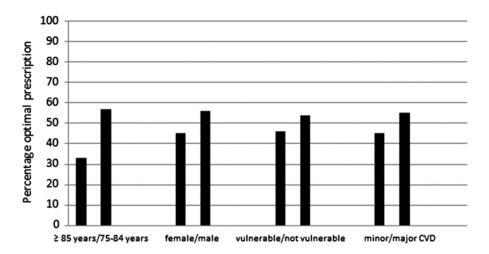


Figure 1. Optimal prescription rates (both lipid-lowering and antithrombotic drugs) depending on age, sex, GPs' judgement of vulnerability, and severity of cardiovascular disease (n = 1350; p all < 0.05).

Table 3. Relation of age, sex, GPs' judgement of vulnerability, and severity of cardiovascular disease with optimal prescription rates of cardiovascular preventive treatment in participants with a history of cardiovascular disease from the ISCOPE study (n = 1350).

	Age ≥ 85 years		Female sex		Vulnerable ²		Minor CVD ³	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Univariate	0.37	0.29-0.48	0.63	0.50-0.78	0.79	0.62-0.99	0.65	0.53-0.81
Multivariate ⁴	0.39	0.30-0.50	0.71	0.57-0.89	0.88	0.69-1.1	0.67	0.53-0.83

CVD: cardiovascular disease. ¹Both lipid lowering and antithrombotic drug; ²patient considered vulnerable by their GP, 12 missing values; ³history of angina, transient ischaemic attack, or claudication without arterial surgery; ⁴adjusted for age, gender, vulnerability, and disease severity.

median age of 81 years. In the high age group, 42% of the participants were treated optimally compared with 58% in the low age group (OR 0.50 [95% CI 0.40–0.62]; multivariate OR 0.53 [0.42–0.66]). When making tertiles of age, we observed optimal treatment in 36% in the highest tertile (age > 83.5 years), in 54% in the middle tertile, and in 61% in the low age tertile (age \leq 79.0 years) (p trend < 0.01), indicating that the influence of age on prescription rates is dose-dependent and robust.

Analyses with regard to vulnerability, excluding the 'possibly vulnerable' participants, did not substantially change the results (univariate and multivariate OR for GPs' judgement of vulnerability 0.74 [95% CI 0.57–0.96] and 0.86 [0.65–1.1], respectively).

The severity of CVD expressed as involvement of more than one vascular bed (n = 214) was positively associated with optimal treatment (optimal prescription in 63% versus 48% for one vascular bed, p < 0.01). Univariate OR for one vascular bed was 0.54 (95% CI 0.40–0.73) and multivariate OR (including age, sex, and GPs' vulnerability judgement) was 0.54 (0.39–0.74).

Stratified analyses performed in the group with a recent cardiovascular disease (< 2 years before the start of the ISCOPE study) and a cardiovascular disease longer ago showed similar rates of optimal, suboptimal, and poor treatment in both subgroups (data not shown).

Discussion

This study on current prescription rates in secondary cardiovascular prevention in older persons in the Dutch general population shows that half of all participants with a history of CVD received optimal treatment, with a combination of a lipid-lowering drug and an antithrombotic drug. Another quarter received an antithrombotic only, indicating that statin use especially is still limited in old age.

GPs' judgement of vulnerability was not independently associated with lower prescription rates, whereas age itself, female sex, and the severity of CVD history were. In view of increasing research on the influence of vulnerability on medical decision-making in old age this is an intriguing finding, indicating that age, sex, and disease severity are essential constituents of the judgement of vulnerability. In other words when taking age, sex, and disease severity into account, GPs judgement of vulnerability does not independently influence prescription rates. This might be seen as a positive finding, indicating that GPs do not a priori withhold treatment in vulnerable patients.

The severity of the history of CVD proved to be relevant, since older persons with major CVD (MI, stroke, arterial surgery) were more often optimally treated. This leaves room for improvement of preventive therapy in

relatively fit patients with only minor CVD, in whom prevention of major events might help preserve their independence.

Age itself was most strongly associated with prescription rates: only a third of participants aged > 85 years received optimal treatment compared with more than half of those aged 75-84 years. This might partly be due to the START criteria [18] and the relative lack of RCT evidence for secondary preventive treatment with statins in patients aged > 85 years [27], lag time to benefit, and/or an increasing number of comorbidities.

Our data do not allow us to conclude whether the observed low prescription rates are the result of appropriate patient-centred medical decision-making, as opposed to forgetfulness or lack of attention from physicians and patients for cardiovascular preventive measures. Therefore, we recommend that GPs regularly monitor their older patients with a history of CVD (especially those with minor CVD) and individually discuss possible preventive treatments.

Strengths and weaknesses

A strength of our study in a population-based sample of CVD patients in general practice is that it reflects current prescription rates in the general older population in the Netherlands. The GP practices in our study were randomly chosen and there were no predefined cardiovascular criteria. Therefore, the observed prescription rates are representative for current general practice. Moreover, including all atherothrombotic CVD (cardiac, cerebral, and peripheral) also allowed us to observe the prescription rates for the whole secondary prevention population and not for a specific vascular bed only.

It is well known that drug prescription rates after incident cardiovascular disease decline over time [15]. However, in our sensitivity analysis in participants with a recent cardiovascular disease (as compared with those with cardiovascular disease longer ago), prescription rates were similar, indicating that the low prescription rates observed in older people are most likely not caused by the fact that cardiovascular disease in general presented itself longer ago in this old population.

Various tools have been developed to screen for vulnerability. GPs' assessment of vulnerability is an easily available parameter in general practice. Since the goal was to assess patient vulnerability as defined by GPs themselves, GPs were not provided with a specific definition of vulnerability. It could be questioned as to which constituents GPs' judgement of vulnerability is based on. Therefore, an in-depth validation study on the vulnerability assessment by GPs within the ISCOPE study was performed by Drewes et al. [28]. This study

concluded that somatic and psychological problems were uniformly taken into account in GPs' judgement of vulnerability.

Another weakness may be that we used routine clinical data and that not all diagnoses were validated by a team of experts. Also, information on the frequency of consultations for secondary cardiovascular prevention in the GP practices was not available, and a possible influence of consultation frequency on prescription rates could therefore not be studied.

A further weakness is that we have no qualitative information on physicians and patients and do not know the reasons for not prescribing medication; moreover, due to small numbers, GP-specific analyses were not possible. Furthermore, it is unknown whether some patients had been prescribed statins in the past and had discontinued taking them, e.g. because of side effects. Also, the use of a more complex and validated frailty or vulnerability instrument might have yielded different results. However, it is still unknown which instrument is best and, in routine practice, GPs use their general and intuitive judgement of vulnerability. Finally, 60% of all eligible patients aged > 75 years in general practices in the Netherlands who were invited to participate in the ISCOPE study did so. However, in the non-response analysis of the ISCOPE study, median age of nonresponders was 81 years, and 25% were considered vulnerable by their GP. Therefore we think including these non-responders would not substantially have changed our results.

Findings in relation to other studies

To our knowledge this is the first study to investigate the association between GPs' judgement of vulnerability and prescription rates of secondary cardiovascular preventive drugs in old age. An association between lower prescription rates of statins and depression/cognitive decline was reported in a retrospective cohort study with a mean age of 74 years [29].

The association between secondary preventive drug treatment and the severity of CVD has seldom been examined. In the EURASPIRE surveys prescriptions of statins increased over time but there was a tendency towards lower prescription rates in participants with ischaemia as compared with patients with CABG, PTCA, or acute MI [30]. However, this was not the main objective of this study, mean age was much younger (around 60 years old), and the study population was confined to cardiac disease patients from specialist cardiac centres, not representing the general population. Also in a younger age group (mean age 70 years),

Bangalore et al. observed reduced secondary preventive treatment in participants with TIA as compared with participants with stroke [25]. As major CVD is associated with poorer prognosis [31], these results may reflect GPs' awareness of this.

With regard to the observed lower prescription rates of secondary preventive medication with increasing age, lower prescription rates after MI have been reported in older age groups [14,15,24,32]. In a meta-analysis, Naderi et al. showed that prescription rates in secondary prevention in age groups with a mean age of 58–78 year were higher (i.e. 66%) for all cardiovascular preventive treatment [33]; this is consistent with our finding that younger age is associated with higher prescription rates. However, the latter authors observed no differences in drug classes in these age groups, whereas in the present study statins were less frequently prescribed than antithrombotics. This might indicate that in very old age statin treatment is not started or is more often discontinued, possibly because of lack of evidence in very old age [18,27], (expected) side effects, or lag time to benefit.

With regard to the observed sex differences, lower prescription rates of lipid-lowering drugs in women in particular are often mentioned [15,24,32]. This might be because most evidence regarding the benefits of treatment with statins was collected in men, and physicians have a lower awareness of the comparable risks for women. However, this sex difference is not favourable for the ageing society, in which more women live to higher ages.

Meaning of the study

In the present study in older people in the general population, rates of secondary cardiovascular preventive drug prescriptions were relatively low; this may increase the risks of recurrent CVD. Since an intensive outpatient cardiac rehabilitation programme recently showed benefits even in patients aged \geq 80 years [34], optimising secondary preventive measures can be worthwhile, even in old age. The observed low prescription rates, especially of statins, in women and in participants with minor CVD, may be the result of a careful decision process weighing all the pros and cons of preventive treatment; however, it may also reflect forgetfulness or loss of attention for these patients. Patients themselves may also have discontinued treatment without their GPs noticing. Therefore, we recommend that physicians regularly monitor all (very) old patients with established CVD for current use of secondary preventive medication, make an explicit analysis, discuss this with their patients and adjust the individual treatment accordingly.

Further research

The present study did not investigate the influence of physicians' and patients' preferences on prescription rates. In primary prevention, Fried et al. observed that older persons' willingness to take medication was relatively insensitive to its benefits, but highly sensitive to its adverse effects [35]. Qualitative research interviewing patients and physicians regarding their opinions on prescription of secondary preventive medication in very old age may further elucidate possible reasons for non-prescription or discontinuation of treatment in this age group.

Conclusion

In old age, only half of all those patients with an indication for secondary preventive cardiovascular medication receive optimal treatment with both lipid-lowering drugs and antithrombotics. Whereas age, female sex, and minor CVD are independently associated with even lower prescription rates, GPs' judgement of vulnerability is not. Because this low treatment uptake may not always be the result of a conscious patient-centred choice, we advocate individual proactive re-evaluation of preventive treatment in all older patients, especially (female) patients with a history of minor CVD.

Acknowledgements

Authors' contributions: PGvP was responsible for study concept and design, analysed and interpreted data, drafted the manuscript, and did statistical analysis. JG was responsible for study concept and design, statistical analysis and interpretation of data, and critical revision of the manuscript for important intellectual content. WPJdE was responsible for study concept and design, acquisition of data, statistical analysis and interpretation of data, and critical revision of the manuscript for important intellectual content. JB was responsible for study concept and design, acquisition of data, statistical analysis and interpretation of data, and critical revision of the manuscript for important intellectual content. MWMdW was responsible for study concept and design, acquisition of data, analysis and interpretation of data, and critical revision of the manuscript for important intellectual content. WdR was responsible for study concept and design, analysis and interpretation of data, and for critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.



This study was funded by ZonMw, the Netherlands, Organization for Health Research and Development: ZonMw No. 311060201. The sponsor had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

References

- 1. Available at http://www.who.int/mediacentre/factsheets/ fs310/en/#
- 2. Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM, et al. Heart disease and stroke statistics - 2011 update: A report from the American Heart Association. Circulation 2011;123:e18-e209.
- 3. Zuckerman IH, Yin X, Rattinger GB, Gottlieb SS, Simoni-Wastila L, Pierce SA, et al. Effect of exposure to evidencebased pharmacotherapy on outcomes after acute myocardial infarction in older adults. J Am Geriatr Soc 2012;60:1854-61.
- 4. Shepherd J, Blauw GJ, Murphy MB, Bollen EL, Buckley BM, Cobbe SM, et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): A randomised controlled trial. Lancet 2002;360:1623-30.
- 5. Deedwania P, Stone PH, Bairey Merz CN, Cosin-Aguilar J, Koylan N, Luo D, et al. Effects of intensive versus moderate lipid-lowering therapy on myocardial ischemia in older patients with coronary heart disease: Results of the Study Assessing Goals in the Elderly (SAGE). Circulation 2007;115:700-7.
- 6. Alhusban A, Fagan SC. Secondary prevention of stroke in the elderly: A review of the evidence. Am J Geriatr Pharmacother 2011:9:143-52.
- 7. Miettinen TA, Pyorala K, Olsson AG, Musliner TA, Cook TJ, Faergeman O, et al. Cholesterol-lowering therapy in women and elderly patients with myocardial infarction or angina pectoris: Findings from the Scandinavian Simvastatin Survival Study (4S). Circulation 1997;96:4211-18.
- 8. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. N Engl J Med 1998:339:1349-57.
- National Guideline Clearinghouse N. European guidelines on cardiovascular disease prevention in clinical practice (version 2012). Available from: http://www.guideline.gov/ content.aspx?f=rss&id=39354
- 10. National Guideline Clearinghouse N. 2012 ACCF/AHA/ ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease. Available from: http://www.guideline.gov/content.aspx?f=rss&id=39380http://www.guideline.gov/content. aspx?f=rss&id=39380
- 11. National Guideline Clearinghouse N. Primary and secondary prevention of cardiovascular disease: Antithrombotic therapy and prevention of thrombosis, 9th ed. American College of Chest Physicians evidence-based clinical practice guidelines. Available from: http://www.guideline.gov/ content.aspx?f=rss&id=35273
- 12. Smith SC, Jr., Benjamin EJ, Bonow RO, Braun LT, Creager MA, Franklin BA, et al. AHA/ACCF secondary prevention

- and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: A guideline from the American Heart Association and American College of Cardiology Foundation. Circulation 2011;124:2458-73.
- 13. Van Peet PG, Drewes YM, de Craen AJ, Gussekloo J, de Ruiiter W. NT-proBNP best predictor of cardiovascular events and cardiovascular mortality in secondary prevention in very old age: The Leiden 85-Plus Study. PLoS One 2013:8:e81400.
- 14. De Ruijter W, de Waal MW, Gussekloo J, Assendelft WJ, Blom JW. Time trends in preventive drug treatment after myocardial infarction in older patients. Br J Gen Pract 2010;60:47-9.
- 15. Koopman C, Vaartjes I, Heintjes EM, Spiering W, van Dis I, Herings RM, et al. Persisting gender differences and attenuating age differences in cardiovascular drug use for prevention and treatment of coronary heart disease, 1998-2010. Eur Heart J 2013;34:3198-205.
- 16. Graversen L, Christensen B, Borch-Johnsen K, Lauritzen T, Sandbaek A. General practitioners' adherence to guidelines on management of dyslipidaemia: ADDITION-Denmark. Scand J Prim Health Care 2010;28:47-54.
- 17. Lee SJ, Leipzig RM, Walter LC. Incorporating lag time to benefit into prevention decisions for older adults. JAMA 2013;310:2609-10.
- 18. O'mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: Version 2. Age Ageing 2015;44:213-18.
- 19. Van Peet P, Drewes Y, Gussekloo J, de Ruijter W. GPs' perspectives on secondary cardiovascular prevention in old age: A focus group study. Br J Gen Pract 2015;65:e739-47.
- 20. Alexander KP, Newby LK, Armstrong PW, Cannon CP, Gibler WB, Rich MW, et al. Acute coronary care in the elderly, part II: ST-segment-elevation myocardial infarction: A scientific statement for healthcare professionals from the American Heart Association Council on Clinical Cardiology: in collaboration with the Society of Geriatric Cardiology. Circulation 2007;115:2570-89.
- 21. Fried TR, Tinetti ME, Iannone L. Primary care clinicians' experiences with treatment decision making for older persons with multiple conditions. Arch Intern Med 2011;171:75-80.
- 22. Drewes YM, Koenen JM, de Ruijter W, van Dijk-van Dijk DJ, van der Weele GM, Middelkoop BJ, et al. GPs' perspectives on preventive care for older people: A focus group study. Br J Gen Pract 2012;62:e765-72.
- 23. Afilalo J, Alexander KP, Mack MJ, Maurer MS, Green P, Allen LA, et al. Frailty assessment in the cardiovascular care of older adults. J Am Coll Cardiol 2014;63:747-62.
- Lee HY, Cooke CE, Robertson TA. Use of secondary prevention drug therapy in patients with acute coronary syndrome after hospital discharge. J Manag Care Pharm 2008;14:271-80.
- 25. Bangalore S, Schwamm L, Smith EE, Singh IM, Liang L, Fonarow GC, et al. Secondary prevention after ischemic stroke or transient ischemic attack. Am J Med 2014;127:728-38.
- 26. Poot AJ, den Elzen WP, Blom JW, Gussekloo J. Level of satisfaction of older persons with their general

- - practitioner and practice: Role of complexity of health problems. PLoS One 2014;9:e94326.
- 27. Strandberg TE, Kolehmainen L, Vuorio A, Evaluation and treatment of older patients with hypercholesterolemia: A clinical review. JAMA 2014;312:1136-44.
- 28. Drewes YM, Blom JW, Assendelft WJ, Stijnen T, den Elzen WP, Gussekloo J. Variability in vulnerability assessment of older people by individual general practitioners: A crosssectional study. PLoS One 2014;9:e108666.
- 29. Benner JS, Glynn RJ, Mogun H, Neumann PJ, Weinstein MC, Avorn J. Long-term persistence in use of statin therapy in elderly patients. 2002;288:455-61.
- 30. Kotseva K, Wood D, De BG, De BD, Pyorala K, Keil U. Cardiovascular prevention guidelines in daily practice: A comparison of EUROASPIRE I, II, and III eight European countries. surveys in 2009;373:929-40.

- 31. Van Peet PG, Drewes YM, de Craen AJ, Westendorp RG, Gussekloo J, de Ruijter W. Prognostic value of cardiovascular disease status: The Leiden 85-plus study. Age (Dordr) 2013;35:1433-44.
- 32. Simpson CR, Hannaford PC, Williams D. Evidence for inequalities in the management of coronary heart disease in Scotland. Heart 2005;91:630-4.
- 33. Naderi SH, Bestwick JP, Wald DS. Adherence to drugs that prevent cardiovascular disease: Meta-analysis on 376,162 Patients. Am J Med 2012;125:882-7.e1.
- 34. Mehta H, Sacrinty M, Johnson D, St CM, Paladenech C, Robinson K. Comparison of usefulness of secondary prevention of coronary disease in patients <80 versus >/ =80 years of age. Am J Cardiol 2013;112:1099-103.
- 35. Fried TR, Tinetti ME, Towle V, O'Leary JR, lannone L. Effects of benefits and harms on older persons' willingness to take medication for primary cardiovascular prevention. Arch Intern Med 2011;171:923-8.