Cholesterol- and blood pressure-lowering drug use for secondary cardiovascular prevention in 2004 - 2013 Europe

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Abstract 243 words; **Manuscript word count** (manuscript text, including title, author names/affiliation, abstract, keywords, figure/table legends and references): 3,845; further 3 Tables and 1 Figure.

Abstract

Background Suboptimal use of cardiovascular prevention medications has been reported. We report recent trends in secondary cardiovascular disease (CVD) prevention drug use in Europe.

Design Study of Health and Retirement in Europe (SHARE), a large longitudinal 2004-2013 cohort study in middle-aged and elderly Europeans.

Methods Cross-sectional and panel logistic regression models were used to study trends in cholesterol- and blood pressure (BP)-lowering drug use and effects of individual characteristics among participants with CVD in SHARE.

Results 21,371 SHARE participants reported cardiovascular disease and, at initial report, 40% and 60% of them used cholesterol- or BP-lowering drugs, respectively. Increasing cross-sectional time trends were observed for both medication classes (odds ratios [OR] of use in 2013 vs 2004, 1.6 [95%CI 1.4-1.7] and 1.5 [1.4-1.6], respectively). However, among individuals with multiple observations, the use of both classes declined over time (2013 vs 2004 OR 0.63 [0.51-0.77] and 0.68 [0.55-0.84]; both trend $p<0.001$), and with increasing duration since last cardiovascular event (OR 0.74 [0.60-0.91], trend $p=0.01$ and OR 0.82 [0.66-1.03], trend $p=0.06$, respectively for durations of 9 years or more versus less than one year). Among people with CVD, those obese, retired or with hypercholesterolemia, hypertension, worse self-perceived health, and, in the case of lipid-lowering medication, with diabetes, were more likely to use these medications.

Conclusions Despite moderately increasing cross-sectional time trends, the use of secondary CVD prevention drugs remains low in Europe with substantial discontinuation over time and with increasing duration from an acute cardiovascular event.

Keywords: cardiovascular disease; cholesterol-lowering drug therapy; blood pressure drug therapy; medication compliance.

INTRODUCTION

For people who have suffered a myocardial infarction or stroke, ample evidence and clinical guidelines support the use of cholesterol- and blood pressure (BP)-lowering drugs to reduce increased risks of further cardiovascular events.[1, 2] However, suboptimal use of these medications has been reported in such populations.[3, 4] A European multi-national cross-sectional study reported national levels of use of cholesterol-lowering medications about one year after the admission to hospital with an acute coronary event ranging from 74% to 96% for statins, of β-blockers from 68% to 94%, and of ACE inhibitors/angiotensin II receptor-blockers from 49% to 87% in 2012-2013.[5] A study of 2007-2010 drug-dispensing records in the Netherlands found that three years after hospital admission for an acute coronary syndrome (ACS) merely 53%, 50% and 57% used lipid-lowering, β-blockers and other BP-lowering drugs, respectively.[6] Variation in use has been reported across gender, age, health and socio-economic status.[3, 6, 7] However, ways of identifying individuals likely to not initiate or to discontinue therapy and strategies to improve use of preventive medications remain understudied.[8] We report recent trends in cholesterol- and BP-lowering drug use for secondary cardiovascular disease (CVD) prevention in middle-aged and older Europeans and factors associated with suboptimal use.

METHODS

The Survey of Health, Ageing and Retirement in Europe (SHARE)

SHARE's design and sampling frame aimed to recruit and follow representative national population samples. Individuals aged 50 or older and their spouses were recruited from 20 European countries and followed in waves 1 [2004-2006], 2 [2007-2009], 4 [2010-2012] and 5 [2013]. Trained personnel led face-to-face computer-assisted personal interviews and conducted anthropometric examinations of the participants during each study wave and data were collected on socio-economic, health and wellbeing factors including medication intake, history of onset of chronic conditions, health-related behaviours and cognitive factors. Further details of the design, survey methods and population characteristics are reported in the supplementary methods.[9]

SHARE participants with history of CVD

For the current analysis, we identified all SHARE participants with self-reported history of doctor-diagnosed CVD. Throughout the study, participants were asked "Has a doctor ever told you that you had any of the conditions…?" followed by a list of common chronic diseases including heart attack (ie, myocardial infarction, coronary thrombosis and congestive heart failure) and stroke or cerebral vascular disease. At each subsequent study interview, participants were also asked if they had suffered a heart attack or stroke since their last interview. Report of any of these conditions was used to determine prior CVD (**Supplementary Table 1**).

Outcomes

Throughout the study, participants provided information on whether they were taking drugs at least once a week for: (i)high blood cholesterol, (ii)high blood pressure, (iii)coronary or cerebrovascular diseases, and (iv)other heart diseases. Two (binary) main outcome variables were established: (i)self-reported use of cholesterol-lowering drugs and (ii)self-reported use of BP-lowering drugs. To assess the impact of a potential misclassification of CVD medications owing to self-reports, a third outcome variable summarising use of any cardiovascular medication (the above two categories plus any drug for coronary, cerebrovascular or other heart disease) was used in sensitivity analyses.

Statistical analyses

First, the relevance of a range of participant characteristics to the likelihood of use of cholesterol- or BP-lowering medication was estimated at participants' initial report of CVD using logistic regression models and adjusting for current age, gender, education and participant country. Second, cross-sectional time trends across study waves (i.e. each wave was considered an independent data snapshot of medication use) were estimated within participating countries, within categories of countries by higher- or lower- median gross national income (GNI) (with threshold of $29,460 [PPP-adjusted in current international $] in 2004[10]) and across all participating countries using logistic regression models. The Wald test for heterogeneity or, if appropriate, trend in drug use between categories of participants was used after adjustment for current age, gender, education and participant country as relevant.[11]

Third, the importance of (i)between-participant variation and (ii)within-participant variation in medication use was investigated using the longitudinal SHARE data. Multivariate panel logistic regression models were estimated including statistically significant participant characteristics from the initial logistic regressions (with current age, gender, education and country preserved independently of statistical significance). Such participant characteristics included marital status, history of hypercholesterolemia, hypertension, diabetes or other chronic conditions, time duration since latest heart attack or stroke, body mass index (BMI), alcohol consumption, smoking, physical exercise, employment, cognitive function, self-perceived health, education, household equivalised income and residential area (for variable definitions see **Supplementary Table 1**). Participants' characteristics were updated throughout the study using the latest questionnaire data. For categorical factors with a small percentage of missing values (<5%), missing values were allocated to the middle category. Where the proportion of missing observations was larger, a further category "missing" was created. The Hausman test was used to compare estimates from a fixed-effects panel logistic model and pooled random-effects panel logistic model and to guide the choice of the appropriate model.[12]

Sensitivity analyses studied whether the results differed between higher- and lower-GNI countries. The impact of possible misreporting of the type or purpose of any used cardiovascular medication was investigated by evaluating relevance of participant characteristics on the reported use of any cardiovascular drug, as well as on the reported combined cholesterol- or BP-lowering drug use.

All statistical analyses were performed with Stata (version 12, Stata Corp, USA).

RESULTS

Study population

109,000 individuals from 20 countries were recruited and followed between 2004 and 2013, of whom 21,371 (20%) reported CVD at any point during the study (16% reported heart attack and 5% stroke). 8,431 (39%) of these participants were interviewed only once and 12,957 (61%) at least twice (39%, 12% and 10% were interviewed twice, thrice and four times, respectively). The mean age at first report of CVD (i.e. baseline) was 72 years (SD 10) and 52% were male (**Table 1**). At baseline, participants reported that they had had CVD for a median of 7 (IQR 2-15) years and had had their

latest heart attack or stroke at a median of 6 (IQR 1-14) years previously; 37% and 57% reported having been told by their doctor that they had high cholesterol or high BP, respectively.

Self-reported use of cholesterol- and BP-lowering medication at initial CVD report in SHARE

Overall, 8,509 (40%) and 12,909 (60%) of the 21,371 participants with CVD reported they were using cholesterol- or BP-lowering medication, respectively, at baseline (**Table 1**). Compared to non-users, users of cholesterol- or, separately, BP-lowering drugs were more likely to be overweight or obese (both trend $p<0.001$ for BMI>18.5kg/m^2), retired (both heterogeneity $p<0.001$), to have diabetes (both $p<0.001$) or other comorbidities (both trend $p<0.001$ across categories of other comorbidities) and to not be a current smoker (both heterogeneity $p<0.001$). Users of cholesterol-lowering drugs were also less likely to be elderly (trend $p<0.001$) or female (37% vs. 42%; $p<0.001$), while the opposite was observed for users of BP-lowering drugs (trend $p<0.001$ across age categories; 64% use in women vs. 57% in men, $p<0.001$). However, the strongest cross-sectional associations were observed between history of high cholesterol and use of cholesterol-lowering drugs (79% vs. 16%, $p<0.001$) and between history of high BP and use of BP- lowering drugs (90% vs. 20%, $p<0.001$; **Table 1**).

Cross-sectional trends in self-reported use of cholesterol- and BP-lowering drugs between 2004 and 2013

After adjustment for participants' age, gender and education, increasing cross-sectional trends in use of cholesterol- and BP-lowering drugs between 2004 and 2013 were observed in most participating countries (**Table 2**). These trends were significant across all participating countries (OR 1.6 [95%CI 1.4-1.7] for cholesterol-lowering drug use and 1.5 [1.4-1.6] for BP-lowering drug use in 2013 compared to 2004-2006; **Table 2, Figure 1**) and separately significant among participants from the higher- and lower-GNI countries (**Table 2, Supplementary Figure 1**).

Participant characteristics associated with self-reported cholesterol- and BP-lowering drug use: longitudinal cohort panel data analysis

The Hausman tests did not support the hypotheses that the differences in coefficients between fixed and random-effects panel logistic models are not systematic ($p<0.001$ for both cholesterol- and BP-

lowering drug use), and the fixed-effects panel model was indicated to account for possible time-invariant confounding.

The results of the longitudinal fixed-effects logistic regression models (**Table 3**) indicated that, similar to the cross-sectional analysis, hypercholesterolemia remained the strongest indicator of cholesterol-lowering medication use (OR 22.9 [95%CI 18.2-28.8]), and hypertension of BP-lowering drug use (OR 36.5 [28.2-47.4]). However, in contrast to the increasing cross-sectional time trends, two concurrent time trends of decreasing drug use were observed at participant level. Firstly, medication use generally declined over time within individuals (p for trend <0.001) for both cholesterol-lowering drugs (2013 vs 2004 OR 0.63 [95%CI 0.51-0.77]) and BP-lowering drugs (OR 0.68 [0.55-0.84]). Secondly, drug use diminished with an increasing duration since the latest cardiovascular event (OR 0.74 [95%CI 0.60-0.91], trend p=0.01 and OR 0.82 [0.66-1.03], trend p=0.06, respectively for durations of "9 years or more" versus "less than one year") (**Table 3**), a discontinuation particularly clear after the first few years following an event. A stronger decline (heterogeneity p<0.001) in drug use over time (2013 vs. 2004) was observed in lower-GNI countries (cholesterol-lowering drug use: OR 0.53 [95%CI 0.38-0.74]; BP-lowering drug use: OR 0.36 [0.25-0.52]) than in higher-GNI countries (cholesterol-lowering drug use: OR 0.68 [0.57-0.80]; BP-lowering drug use: OR 0.91 [0.70-1.20]) (**Supplementary Table 2**).

Compared to those of normal weight, obese participants (BMI≥30) were more likely to take cholesterol- (OR 1.38 [95%CI 1.02-1.86]) and BP-lowering drugs (OR 1.52 [1.12-2.08]; **Table 3**). Similarly, participants with poorer self-perceived health had a higher propensity to use cholesterol- (OR 1.84 [95%CI 1.49-2.29]) and BP-lowering drugs (OR 2.25 [1.82-2.79]) compared to those rating their health as excellent or very good. Participants aged 68-77 were more likely to use cholesterol-lowering drugs than younger participants (OR 1.32 [1.08 -1.62]). Retirement was associated with an increase in usage of both medications (cholesterol-lowering drug use: OR 1.96 [95%CI 1.49-2.57]; BP-lowering drug use: OR 1.80 [1.35-2.40]) independently of age. Diagnosis of diabetes was associated with increased odds of cholesterol-lowering drug use (OR 1.57 [95%CI 1.21-2.05]); however, an increasing number of other comorbidities did not affect drug use. Changes in cognitive function, alcohol consumption, smoking behaviour, frequency of physical exercise, marital status, and

household income were not associated with changes in drug use. No differences in drug use were observed between rural versus urban residences.

In the sensitivity analysis, while the temporal trends for use of any cholesterol- or BP-lowering medication remained positive (**Supplementary Table 3**), there was no evidence for cross-sectional temporal trends in use of any cardiovascular drug (**Supplementary Table 4**). The longitudinal fixed-effect panel model of use of any cardiovascular drug produced results largely consistent with the results for cholesterol- and BP-lowering drug use, with even stronger trends of decreasing medication use within individuals with increasing duration since the latest cardiovascular event. The associations of hypertension and hypercholesterolemia with any cardiovascular medication use were much weaker compared to associations with cholesterol- or BP-lowering drug use (**Supplementary Table 5**).

DISCUSSION

In this longitudinal, community-based study of use of cholesterol- and BP-lowering drugs for secondary CVD prevention in a middle-aged and elderly European population, cross-sectional analyses showed that the use of both categories of medication was low (40% and 60%, respectively, at initial CVD report) and increased only moderately from 2004 to 2013. Further analysis among participants with multiple observations showed that the use of both drug categories declined (i) over time, and (ii) with an increasing number of years since the latest cardiovascular event. History of doctor-diagnosed hypercholesterolemia and hypertension were the strongest predictors of usage of cholesterol- and BP-lowering medications, respectively. Retirement, low self-perceived health, diabetes and obesity were positively associated with medication use.

Since the late 1990s, (inter)national clinical guidelines have progressively recommended a shift away from cholesterol and BP levels as factors determining the need for preventive CVD drug treatments and towards an approach targeting absolute cardiovascular risk.[13-16] Our study in a large community-based middle-aged and elderly European population draws a picture of preventive cardiovascular drug use and complements other survey data[17]. Its longitudinal nature allowed us to study factors associated with suboptimal preventive drug use and, with one-third of the participants aged 77 years or over, the study also provides valuable insights into the understudied elderly population.

The perceived disease risk appears an important factor even in a population with established CVD. While, independently of their cholesterol and BP levels, virtually all participants should be treated to prevent further CVD events, those patients with doctor-diagnosed hypertension and hypercholesterolemia had a 4.5 and 4.6 times greater probability of being on BP and cholesterol-lowering medications, respectively, than people with CVD but without such conditions. Similar observations have been made in a Chinese CVD population[18], an international survey[4] and a U.S. coronary disease population.[19] Furthermore, individuals with good self-perceived health, without diabetes, still in employment and/or not obese were less likely to use drugs despite having established CVD. However, our study data does not allow distinguishing between suboptimal prescribing and individuals' lack of compliance.

We found evidence for increasing cross-sectional time trends of cholesterol-and BP-lowering drug usage both in lower- and higher-income European countries. The probability of being on cholesterol- and BP-lowering medication increased from 34% and 54% in 2004-2006 to 43% and 63% in 2013, respectively. The EUROASPIRE surveys in individuals about one year post an acute coronary hospital admission showed that between 2006 and 2013, crude statin and β-blocker use rose from 78% to 86% and from 80% to 83%, respectively.[5, 20] A population-based study of dispensing records in the Netherlands also found drug use at three years after discharge for ACS increased from 36% to 53% for lipid-lowering drugs and from 41% to 50% for β-blockers between 1998 and 2007[6]. These positive trends at the macro-level suggest that clinical guidelines have been progressively translated into practice. However, large variations still exist between countries with those with lower GNI making slower progress than their wealthier counterparts.

The likelihood of discontinuing use of cardiovascular medication at individual level is worrisome. Individuals in our study appear to increasingly discontinue treatment over time as well as with increasing duration since their latest cardiovascular event. The usage rates in the study, about 6 year after event, are also substantially lower than rates in the EUROASPIRE survey, about one year after an acute event. Other studies have also reported diminishing use of these medications with time from initiation. A study of separate, population-based cohorts with acute and chronic coronary disease reported that only 40% and 36%, respectively, were adherent to statin therapy two years following

treatment initiation,[21] while, the proportion of medication-adherent elderly population declined to 32% ten years after statin initiation in another study.[22] While effective and affordable methods to improve adherence to medication regimens and to clinical guidelines are required, there is a striking lack of evidence of effective and cost-effective interventions, and most such experimental studies have too short follow-up periods to evaluate long-term outcomes.[23] A number of possible study limitations should be acknowledged. First, given the survey questions, it is not possible to differentiate between medication prescribing and intake. Second, the survey question regarding prior heart disease was broad and could include heart failure; however, we expect that the numbers with heart failure were relatively small. Finally, the use of categories of medication was derived from patient self-reports, which may be subject to misclassification. It cannot be excluded, for instance, that respondents regarded their cholesterol- or BP-lowering medication as cerebrovascular or other heart disease medication. However, any misclassification is likely to hold over time and within individuals and would be unlikely to bias our conclusions regarding impact of participant characteristics on drug use as confirmed by the sensitivity analyses. While we cannot rule out that the cross-sectional trends in cholesterol- and BP-lowering drugs use might be affected by misclassification, a recent study with validated pharmaceutical record linkage data reported very similar drug utilisation rates.[6]

Conclusion

Health gains could be substantially increased with improved use of effective and widely available cholesterol- and BP-lowering medications. Both physician- and patient-centred measures should be taken and more methodologically sound research and new strategies to improve adherence are needed.

Supplementary material

Supplementary material enclosed

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Conflicts of Interest: None

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Table 1 Characteristics of the 21 371 SHARE participants with history of CVD, overall and by self-reported use of cholesterol- and BP-lowering drugs at baseline

Participant characteristic*		All participants n=21 371 n	Cholesterol-lowering drug users n=8 509 (40%) n (%)		Test for heterogeneity/ trend† p-value	BP-lowering drug users n=12 909 (60%) n (%)		Test for heterogeneity/ trend† p-value
Age (years):	≤ 67	8125	3381	(42)	<0.001‡	4564	(56)	<0.001‡
	68-77	7238	3069	(42)		4645	(64)	
	+77	6008	2059	(34)		3700	(62)	
Gender:	Male	11190	4719	(42)	<0.001	6422	(57)	<0.001
	Female	10181	3790	(37)		6487	(64)	
Hypertension:	Yes	12231	5804	(47)	<0.001	11068	(90)	<0.001
	No	9140	2705	(30)		1841	(20)	
Hypercholesterolemia:	Yes	7934	6295	(79)	<0.001	5736	(72)	<0.001
	No	13437	2214	(16)		7173	(53)	
Diabetes:	Yes	4594	2482	(54)	<0.001	3456	(75)	<0.001
	No	16777	6027	(36)		9453	(56)	
Other co morbidities:	None	7697	2985	(39)	<0.001‡	4334	(56)	<0.001‡
	1	7065	2769	(39)		4316	(61)	
	2-9	6609	2755	(42)		4259	(64)	
Time since latest heart attack/ stroke (years):	0-1	5197	2114	(41)	0.814‡	3173	(61)	<0.029‡
	2-4	3324	1352	(41)		1981	(60)	
	5-9	3855	1580	(41)		2292	(59)	
	+9	7813	3050	(39)		4747	(61)	
	Missing	1182	413	(35)		716	(61)	
Self-perceived health:		1458	577	(40)	<0.001‡	655	(45)	<0.001‡

Excellent/very good							
Good	5203	2070	(40)		2685	(52)	
Fair/poor	14710	5862	(40)		9569	(65)	
Cognitive function (word memorisation): 0-3 words	8696	3286	(38)	0.005‡	5337	(61)	0.690‡
4-5 words	7151	2974	(42)		4409	(62)	
6-10 words	4692	1985	(42)		2666	(57)	
Missing	832	264	(32)		497	(60)	
Body mass index: < 18.5	261	53	(20)	<0.001‡	101	(39)	<0.001‡
≥18.5, < 25	6358	2180	(34)		3167	(50)	
≥25, <30	9454	3926	(42)		5779	(61)	
≥30	5298	2350	(44)		3862	(73)	
Alcohol consumption: not at all to twice/ month	13422	5046	(38)	0.016‡	8448	(63)	0.003‡
1-4/week	4024	1735	(43)		2277	(57)	
≥5/week	3925	1728	(44)		2184	(56)	
Smoking status: Currently smoking	3286	1284	(39)	<0.001§	1722	(52)	<0.001§
Not smoking	11163	4136	(37)		6996	(63)	
Stopped smoking	6922	3089	(45)		4191	(61)	
Frequency of physical exercise: More than weekly	4521	1899	(42)	0.091‡	2432	(54)	<0.001‡
Once a week	2137	815	(38)		1262	(59)	
One to three times a month	1556	544	(35)		877	(56)	
Hardly ever, or never	13157	5251	(40)		8338	(63)	
Employment: Retired	15272	6103	(40)	<0.001§	9568	(63)	<0.001§
Employed or self-employed	2332	890	(38)		1120	(48)	
Unemployed	404	151	(37)		200	(50)	

Permanently sick/ disabled	1480	664	(45)		888	(60)	
Other (homemaker)	1883	701	(37)		1133	(60)	
Marital status:							
Married/ partnership	14546	6128	(42)	<0.001	8726	(60)	0.106
Never married/ divorced/ widowed	6825	2381	(35)		4183	(61)	
Education: None/primary	6609	2571	(39)	0.297‡	4030	(61)	<0.001‡
Secondary	11439	4531	(40)		7019	(61)	
Tertiary	3323	1407	(42)		1860	(56)	
Household income:							
< Half median	3222	1212	(38)	0.04‡	2062	(64)	0.780‡
Half median to median	3456	1262	(37)		2126	(62)	
Median to twice median	1427	609	(43)		843	(59)	
≥ Twice median	371	160	(43)		203	(55)	
Missing	12895	5266	(41)		7675	(60)	
Gross national income (GNI) per capita‖: Lower	11052	3974	(36)	<0.001	7161	(65)	<0.001
Higher	10319	4535	(44)		5748	(56)	
Residential area: Urban	15399	6274	(41)	0.848	9294	(60)	0.79
Rural	5972	2235	(37)		3615	(61)	

Row percentages (from all participants) presented. BP, blood pressure. SHARE, Study of Health and Retirement in Europe.*at first report of prior myocardial infarction or stroke in SHARE.† adjusted for age, gender, education and country, if applicable.‡ test for trend.§ test for heterogeneity.‖ compared to median GNI across countries.

Table 2 Use of cholesterol- and BP-lowering drugs among participants with history of cardiovascular disease in SHARE (n=21,371)

	Users of cholesterol-lowering drugs (%)				p-value for temporal trend*	Users of BP-lowering drugs (%)				p-value for temporal trend*
	2004/06	2007/09	2010/12	2013		2004/06	2007/09	2010/12	2013	
Higher-GNI per capita	**1148 (38)**	**1465 (42)**	**2274 (47)**	**3066 (46)**	**<0.001**	**1459 (49)**	**1907 (55)**	**2790 (58)**	**3944 (60)**	**<0.001**
Austria	49 (24)	81 (35)	304 (36)	289 (34)	0.042	115 (56)	141 (61)	512 (61)	546 (63)	0.033
Belgium	281 (46)	293 (46)	501 (54)	578 (55)	<0.001	247 (40)	352 (55)	534 (58)	601 (57)	<0.001
Denmark	77 (35)	196 (47)	218 (59)	388 (56)	<0.001	112 (51)	244 (59)	232 (63)	431 (63)	0.004
France	190 (39)	200 (40)	462 (47)	390 (43)	0.02	245 (51)	251 (50)	540 (55)	490 (54)	0.113
Germany	116 (28)	134 (30)	135 (42)	371 (40)	<0.001	232 (56)	261 (59)	217 (67)	630 (68)	<0.001
Ireland	NA	64 (59)	NA		NA	NA	71 (65)	NA	NA	NA
Luxembourg	NA	NA	NA	121 (58)	NA	NA	NA	NA	111 (53)	NA
Netherlands	181 (44)	207 (49)	266 (53)	407 (55)	<0.001	184 (45)	206 (49)	271 (54)	409 (55)	<0.001
Sweden	216 (38)	236 (40)	223 (46)	365 (44)	0.021	270 (48)	307 (53)	305 (63)	528 (63)	<0.001
Switzerland	38 (40)	54 (36)	165 (44)	157 (42)	0.537	54 (57)	74 (50)	179 (48)	198 (53)	0.723
Lower-GNI per	**615 (39)**	**1176 (39)**	**2168 (34)**	**2366 (38)**	**<0.001**	**943 (60)**	**1904 (63)**	**4250 (67)**	**4136 (67)**	**<0.001**

capita										
Czech Republic	NA	152 (31)	480 (40)	563 (43)	<0.001	NA	305 (61)	816 (68)	897 (69)	0.002
Estonia	NA	NA	432 (23)	503 (27)	<0.001	NA	NA	1211 (65)	1260 (67)	0.045
Greece	107 (26)	146 (31)	NA	NA	0.019	212 (52)	262 (56)	NA	NA	0.191
Hungary	NA	NA	274 (35)	NA	NA	NA	NA	580 (74)	NA	NA
Israel	316 (61)	435 (68)	NA	369 (64)	0.59	358 (69)	467 (73)	NA	420 (73)	0.878
Italy	94 (29)	152 (32)	204 (34)	304 (37)	0.002	205 (64)	316 (66)	418 (69)	568 (70)	0.052
Poland	NA	180 (30)	183 (37)	NA	0.005	NA	371 (63)	332 (67)	NA	0.089
Portugal	NA	NA	169 (57)	NA	NA	NA	NA	201 (68)	NA	NA
Slovenia	NA	NA	155 (34)	183 (29)	0.094	NA	NA	305 (66)	395 (63)	0.171
Spain	98 (31)	111 (33)	271 (45)	444 (45)	<0.001	168 (53)	183 (54)	387 (64)	596 (60)	0.01
Total	**1763 (39)**	**2641 (41)**	**4442 (40)**	**5432 (42)**	**<0.001**	**2402 (53)**	**3811 (59)**	**7040 (63)**	**8080 (63)**	**<0.001**

BP, blood pressure; GNI, gross national income; NA, not applicable. SHARE, Study of Health and Retirement in Europe.

*adjusted for age, gender, education and country, if applicable.

Table 3 Determinants of use of cholesterol- and BP-lowering drugs in individuals with history of cardiovascular disease: a multivariate fixed-effects panel logistic regression

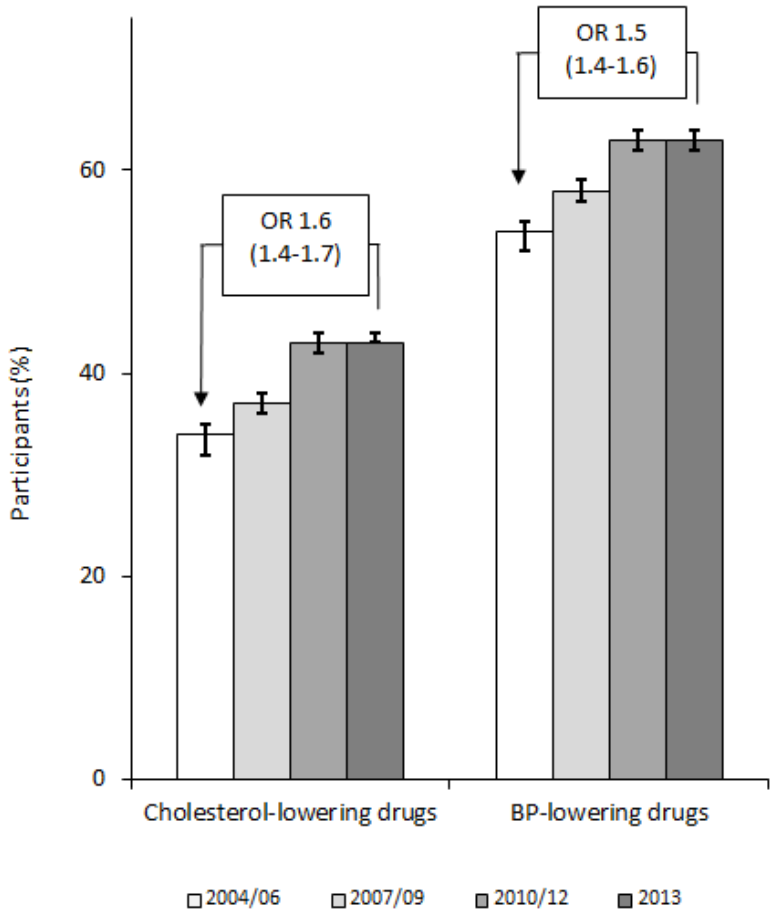
Participant characteristics†	Cholesterol-lowering, n=11 326‡ OR (95% CI)	BP-lowering, n=10 995‡ OR (95% CI)
Age (years) (referent: ≤ 67)		
68-77	1.32 (1.08-1.62)**	1.2 (0.96-1.50)
+77	1.17 (0.86-1.59)	0.85 (0.61-1.19)
Hypertension	1.36 (1.12-1.65)**	36.5 (28.2-47.4)***
Hypercholesterolemia	22.9 (18.2-28.8)***	1.48 (1.19-1.84)***
Diabetes	1.57 (1.21-2.05)***	1.17 (0.89-1.54)
Other comorbidities (referent: None)		
1	1.04 (0.88-1.23)	1.12 (0.94-1.34)
2-9	1.07 (0.86-1.34)	1 (0.79-1.26)
Time since latest heart attack/ stroke (years) (referent: 0-1)		
2-4	1.01 (0.84-1.21)	0.83 (0.67-1.01)
5-9	0.79 (0.65-0.97)*	0.79 (0.63-0.98)*
+9	0.74 (0.60-0.91)**	0.82 (0.66-1.03)
Missing	0.44 (0.39-0.51)***	0.67 (0.59-0.77)***
Self-perceived health (referent: Excellent/very good)		
Good	1.5 (1.21-1.80)***	1.7 (1.37-2.04)***
Fair/poor	1.84 (1.49-2.29)***	2.25 (1.82-2.79)***
Cognitive function (word memorisation) (referent: 6-10 words)		
0-3 words	0.86 (0.73-1.02)	0.84 (0.70-1.00)*
4-5 words	0.96 (0.83-1.11)	0.98 (0.84-1.14)
Missing	0.52 (0.38-0.71)***	0.52 (0.38-0.72)***
Body mass index (referent: ≥18.5, <25)		

<18.5	0.72 (0.29-1.78)	0.65 (0.31-1.37)
≥25, <30	1.09 (0.88-1.35)	1 (0.81-1.25)
≥30	1.38 (1.02-1.86)*	1.52 (1.12-2.08)**
Alcohol consumption (referent: >5/week)		
not at all - twice/month	0.87 (0.72-1.05)	0.98 (0.81-1.20)
1-4/week	1.1 (0.91-1.33)	1.03 (0.85-1.26)
Smoking status (referent: Currently smoking)		
Never smoked	0.56 (0.034-9.33)	0.2 (0.0098-3.99)
Stopped smoking	0.22 (0.0084-5.98)	1.31 (0.032-53.8)
Frequency of physical exercise (referent: More than weekly)		
Once a week	0.94 (0.79-1.14)	0.92 (0.76-1.12)
One to three times a month	0.97 (0.79-1.20)	0.98 (0.78-1.22)
Hardly ever, or never	1.02 (0.88-1.18)	1.11 (0.95-1.30)
Employment (referent: Employed or self-employed)		
Retired	1.96 (1.49-2.57)***	1.8 (1.35-2.40)***
Unemployed	1.37 (0.79-2.36)	1.19 (0.66-2.15)
Permanently sick or disabled	1.74 (1.22-2.47)**	1.33 (0.92-1.92)
Other (homemaker)	1.66 (1.17-2.34)**	1.23 (0.86-1.77)
Marital status (referent: Married/ partnership)		
Never married/divorced/widowed	1.29 (0.94-1.78)	1.06 (0.75-1.49)
Household income (referent: < Half country median)		
Half median to median	1.11 (0.92-1.34)	1.01 (0.83-1.23)
Median to double median	1.05 (0.83-1.34)	1.07 (0.83-1.37)
≥Double median	0.79 (0.53-1.16)	0.9 (0.59-1.37)
Missing	1.05 (0.90-1.22)	0.95 (0.81-1.12)
Residential area (referent: Urban)		
Rural	1.04 (0.84-1.30)	0.93 (0.74-1.18)

Time trend (referent: SHARE wave 1)		
SHARE wave 2	0.7 (0.61-0.80)***	0.79 (0.69-0.91)***
SHARE wave 4	1.16 (0.98-1.39)	1.08 (0.90-1.29)
SHARE wave 5	0.63 (0.51-0.77)***	0.68 (0.55-0.84)***

BP, blood pressure; OR, odds ratio; CI, confidence interval. SHARE, Study of Health and Retirement in Europe. *p<0.05; **p<0.01; ***p<0.001. †Effects of gender and educational attainment cannot be estimated in fixed–effects panel model as they do not change during the study. ‡Fixed-effects panel model excludes individuals without variation in their medication use during the study; with one observation only; or from countries that participated only once in SHARE.

Figure 1 Self-reported use of cholesterol- and BP-lowering drugs (2004/06-2013) among SHARE participants with CVD (n= 21 371)



BP, blood pressure; OR, odds ratio.

Drug use percentages adjusted for age, sex, education and country.