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ORIGINAL RESEARCH ARTICLE

Prevalence and Determinants of the Use of Lipid-Lowering Agents in a Population of Older Hospitalized Patients: the Findings from the REPOSI (REgistro POliterapie Società Italiana di Medicina Interna) Study

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Abstract

Background Older patients are prone to multimorbidity and polypharmacy, with an inherent risk of adverse events and drug interactions. To the best of our knowledge, available information on the appropriateness of lipid-lowering treatment is extremely limited.

Aim The aim of the present study was to quantify and characterize lipid-lowering drug use in a population of complex in-hospital older patients.

Methods We analyzed data from 87 units of internal medicine or geriatric medicine in the REPOSI (Registro Politerapie della Società Italiana di Medicina Interna) study, with reference to the 2010 and 2012 patient cohorts. Lipid-lowering drug use was closely correlated with the clinical profiles, including multimorbidity markers and polypharmacy.

Results 2171 patients aged >65 years were enrolled (1057 males, 1114 females, mean age 78.6 years). The patients treated with lipid-lowering drugs amounted to 508 subjects (23.4%), with no gender difference. Atorvastatin (39.3%) and simvastatin (34.0%) were the most widely used statin drugs. Likelihood of treatment was associated with polypharmacy (≥5 drugs) and with higher Cumulative Illness Rating Scale (CIRS) score. At logistic regression analysis, the presence of coronary heart disease, peripheral vascular disease, and hypertension were significantly correlated with lipid-lowering drug use, whereas age showed an inverse correlation. Diabetes was not associated with drug treatment.

Conclusions In this in-hospital cohort, the use of lipid-lowering agents was mainly driven by patients' clinical history, most notably the presence of clinically overt manifestations of atherosclerosis. Increasing age seems to be associated with lower prescription rates. This might be indicative of cautious behavior towards a potentially toxic treatment regimen.

Key Points

Use of lipid-lowering drugs is a critical issue in older patients.

In a large cohort of hospitalized elderly patients, lipid-lowering drug use was found to be mainly associated with the personal cardiovascular history of patients, and to correlate negatively with age.

1 Introduction

Drug treatment in older patients has been a controversial issue by virtue of a high risk of adverse drug reactions, a high prevalence of polypharmacy, and the inherent risk of drug interactions. This mainly applies to older age strata

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[1, 2], and particularly to hospitalized patients. In this context, treatment with agents aimed to reduce cardiovascular risk, such as hypolipidemic agents, frequently represents a challenge owing to the difficulty of assessing cardiovascular risk in this population.

Indeed, age can be seen as the main risk factor for cardiovascular events in the older decades of the population. Still, the impact of high circulating lipid levels tends to weaken with advancing age [3, 4]. Serum cholesterol increases with aging [3, 5], and a trend toward a plateau after the age of 80 years has been suggested [6, 7]. The pathophysiological alterations underlying such modifications have not been completely understood [8]. A reduction of LDL turnover with ongoing age has been described in males [9] and a recent report using serum sterol precursors has shown a progressive reduction in cholesterol synthesis markers [6, 7]. Subtle alterations in hormonal profile and molecular control of sterol metabolism are likely to underlie such changes [10]. Altogether, these reports support the view of a reduction in the different cholesterol input pathways, which may be related to reduced metabolic needs.

The indication for lipid-lowering treatment in older patients has generated lively debate [11–13], and its management requires careful cost-benefit analysis in terms of side effects and drug interactions [14]. Important alterations in pharmacodynamic and pharmacokinetic profiles have been clearly outlined [15]. Thus, the potential for drug–drug interaction is both highly relevant and considerable for drugs frequently taken by older patients, such as macrolide antibiotics, antifungal agents, and several cardiovascular drugs [16]. Furthermore, the literature documenting the effects of lipid-lowering agents, in particular statins in the elderly, is quite limited due to recurrent exclusion of these patients from clinical trials [17–19]. Information on the actual use of these drugs in general clinical practice is also scarce. It is generally believed, however, that such patients tend to be undertreated even in conditions of high risk [20].

Observational studies can play a pivotal role in that regard, allowing analysts to describe ‘real life’ behaviors. The REPOSI (REgistro POliterapie Società Italiana di Medicina Interna) study was designed as a collaboration between the Italian Society of Internal Medicine and the Mario Negri Institute of Pharmacological Research for the purpose of creating a network of Internal Medicine and Geriatrics wards, allowing for the analysis of drug prescription and polypharmacy in a large population. The specific objective of this analysis was to quantify the use of lipid-lowering drugs, with statins as a primary focus. In addition, our aim was to describe the anamnestic and clinical determinants of their prescription, both in primary and in secondary prevention, within the REPOSI cohort. Special attention was devoted to the association with specific clinical profiles and disease patterns. Such an analysis might indirectly offer insights into the appropriateness of drug prescription in real-life settings.

2 Patients and Methods

2.1 Study Population

The characteristics of patient recruitment and data collection within the REPOSI database have been described in detail elsewhere [21, 22]. The present study included the data of the patients recruited from 87 units of general internal medicine or geriatric medicine in the REPOSI registry in the 2010 and 2012 cohorts. All patients were hospitalized, older than 65 years of age, and able to provide an informed consent. This sample appears to be largely representative of the real-life patient population actually present in the hospital wards in Italy.

The variables collected in the database included diagnosis at admission, socio-demographic information, pharmacological treatment, the main laboratory parameters, the Comorbidity Index according to the Cumulative Illness Rating Scale (CIRS) score [23], the basic activities of daily living according to the Barthel Index [24], cognitive decline using the Short Blessed Test (SBT) [25] in all patients for whom the test was feasible, depression according to the Geriatric Depression Scale, clinical events within hospital stay whenever applicable, diagnosis, and pharmacological treatment at discharge. Recorded data were collected and reclassified by the Mario Negri Institute of Pharmacological Research, Milan, Italy.

The design of the protocol was approved by the Ethical Committee of the province of Modena and the study was performed in accordance with the Declaration of Helsinki in its latest version.

2.2 Diagnosis and Pharmacological Treatment

Diagnosis was posed according to standardized criteria, utilizing the International Classification of Diseases—Ninth Revision (ICD-9) issued by the World Health Organization.

In the present study, the following disease categories and sub-categories were taken into consideration, according to the ICD-9 codes: 250 (diabetes mellitus), 272 (hyperlipidemia), 401–405 (arterial hypertension and inherent complications), 410–414 (coronary heart disease), 428 (heart failure), 430–438 (cerebrovascular disease), and 440–443 (peripheral vascular disease). Patients with a history of coronary, cerebrovascular, or peripheral vascular disease were considered to be in secondary prevention.

All drugs taken at the time of admission were recorded and classified according to the Anatomical Therapeutic Chemical (ATC) classification system (World Health Organization, 1990), which subdivides pharmacological principles on the basis of their target organ or system, and by their chemical and therapeutic properties. Polypharmacy was defined as the use of five or more drugs, which is consistent with the currently accepted criteria in the literature [26, 27], excluding lipid-lowering agents.

The prescription of lipid-lowering agents, as defined by the ATC code C10, was assessed retrospectively and the disease conditions requiring such treatment were considered, consistent with the indications of the Italian regulatory agency (Agenzia Italiana del Farmaco—AIFA, note 13). In the present study, the following pharmaceutical preparations were considered, according to the ATC codes: C10AA, statins (C10AA01, simvastatin; C10AA02, lovastatin; C10AA03, pravastatin; C10AA04, fluvastatin; C10AA05, atorvastatin; C10AA06, rosuvastatin); C10AB, fibric acid derivatives (C10AB05, fenofibrate); C10AC, ionic exchange resins (C10AC01, cholestyramine); C10AX, others (C10AX06, ethyl esters of polyunsaturated omega-3 fatty acids); C10BA, associations (C10BA02, simvastatin plus ezetimibe).

2.3 Calculation of Cardiovascular Risk

The algorithm of the SCORE (Systematic COronary Risk Evaluation) project, where the risk of fatal cardiovascular events at 10 years is evaluated, was utilized; the SCORE O.P. model, which only included people older than 65 years, was adopted [28]. Pertinent variables were inserted into the risk function, and multiplied by the appropriate logistic regression coefficient. The parameters for low-risk European regions were considered. The continuous variables considered by the algorithm were age, systolic arterial pressure, and total cholesterol. The categorical variables were gender, diabetes, and cigarette smoking. Because the risk function only considers patients in primary prevention, patients with a history of previous cardiovascular events were excluded from the statistical analyses that included cardiovascular risk estimation.

2.4 Statistical Analysis

Variables were reported as mean ± SD, or median value with 5–95% confidence interval (5–95% CI), as appropriate.

The significance of differences between normally distributed variables was assessed by means of Student's *t* test for independent data.

The differences between proportions were evaluated by the Chi square test.

Standard logistic regression analysis was performed in order to assess the variables significantly associated with lipid-lowering drug consumption. Stepwise logistic analysis was also performed, where the output is outlined according to the strength of the association. Using this algorithm an exit check of statistical significance is also performed allowing the elimination of the variables with a low degree of significance.

Statistical analysis was performed by means of the SPSS statistical package (version 17 for Windows; SPSS Inc. Chicago, IL, USA), on a PC-IBM compatible workstation; p values <0.05 were considered statistically significant.

3 Results

The population of the 2010 and 2012 REPOSI cohorts included a total of 2703 patients; 532 of them were excluded from analysis because of data incompleteness, leading to a final sample of 2171 enrolled patients (1057 males, 48.7%; 1114 females, 51.3%).

The main clinical characteristics of the analyzed cohort are illustrated in Table 1. As shown, female patients tended to be older whereas male patients presented a higher percentage of polypharmacy (5 or more drugs) and a higher percentage with a clinical history of a previous cardiovascular event. In this cohort, 508 patients (23.4% of the enrolled population, 252 males and 256 females) were receiving lipid-lowering treatment; among them, 468 (92.1%) were receiving a statin, alone or in association with ezetimibe (14 patients), 12 (2.4%) were taking a fibrate (fenofibrate as the only drug), 7 (1.4%) received cholestyramine and 52 (10.2%) were under treatment with polyunsaturated omega-3 fatty acids. Thirty-one patients were receiving a statin and omega-3 fatty acids in association. No gender differences were evident in terms of drug treatment. The vast majority of treated patients were in concomitant treatment with cardiovascular drugs, mainly ACE-inhibitors or sartans (74%), diuretics (67%), antiaggregants (56%), β-blockers (48%), and calcium-channel antagonists (28%); the prevalence of treatment with proton-pump inhibitors was high (37%), whereas coadministration with macrolide or antifungal agents was negligible.

The proportion of lipid-lowering treatment was higher in patients in secondary prevention, compared with those in primary prevention (31.9 vs 16.6%), and so was the percentage of statin treatment (29.4 vs 15.3%) ($p < 0.001$ for both analyses, Chi square test) even if the percentage of patients receiving treatment was relatively low. Taking into consideration statin monotherapy separately, the majority of patients were receiving atorvastatin (40.5%) or simvastatin (33.0%); smaller percentages of patients were

Table 1 Clinical characteristics of the studied sample

Variable	Total (2171)	Males (1057)	Females (1114)
Age (mean ± SD)	78.6 ± 7.3	77.5 ± 6.9	79.7 ± 7.5
Systolic blood pressure (mean ± SD)	130.3 ± 17.3	129.6 ± 17.4	131.0 ± 17.3
Total cholesterol (mean ± SD)	161.7 ± 43.3	154.0 ± 41.7	169.0 ± 43.6
Number of diseases (median, 5–95% CI)	5 (2–11)	6 (2–11)	5 (2–11)
Polypharmacy (≥5 drugs)	1282 (59.1%)	661 (62.5%)	621 (55.7%)
CIRS SI (mean ± SD)	1.65 ± 0.32	1.68 ± 0.33	1.63 ± 0.32
Previous cardiovascular disease	964 (44.4%)	511 (48.3%)	453 (40.7%)
Short Blessed test (mean ± SD)	9.2 ± 8.2	8.4 ± 7.8	9.9 ± 8.5
Barthel index (mean ± SD)	77.0 ± 30.0	80.1 ± 27.9	74.1 ± 31.7

CI confidence interval, *CIRS SI* Cumulative Illness Rating Scale, Severity Index, *SD* standard deviation

Table 2 Clinical characteristics of the studied sample, subdivided on the basis of the documentation of treatment with statins, including the association with ezetimibe

Variable	Treated	Untreated	*p* value
Age (mean ± SD)	78.1 ± 7.0	78.7 ± 7.4	$*p = 0.095$[a]
Systolic blood pressure (mean ± SD)	131.1 ± 16.9	130.1 ± 17.5	NS ($p > 0.10$)[a]
Total cholesterol (mean ± SD)	155.1 ± 40.8	163.5 ± 43.8	$***p < 0.001$[a]
Polypharmacy (≥5 drugs)	81.6%	52.8%	$***p < 0.001$[b]
Barthel index	79.0 ± 27.8	76.5 ± 30.6	$*p = 0.094$[a]
CIRS SI (mean ± SD)	1.74 ± 0.33	1.63 ± 0.32	$***p < 0.001$[a]
CIRS CI (mean ± SD)	3.43 ± 1.89	2.90 ± 1.77	$***p < 0.001$[a]
Previous cardiovascular disease	284 (60.7%)	184 (39.3%)	$***p < 0.001$[b]

CIRS SI Cumulative Illness Rating Scale, Severity Index, *CIRS CI* Cumulative Illness Rating Scale, Comorbidity Index, *NS* non-significant, *SD* standard deviation

* Almost significant ($0.05 < p < 0.10$)

** Significant ($0.01 < p < 0.05$)

*** Highly significant ($p < 0.01$)

[a] Student's *t* test for unpaired data

[b] Chi square test

taking rosuvastatin (18.0%), pravastatin (6.6%), lovastatin (1.1%), or fluvastatin (0.7%).

Supplementary Table 1 (see electronic supplementary material [ESM]) shows the prevalence of cardiovascular disease and of metabolic conditions associated with higher cardiovascular risk (diabetes, dyslipidemia) in the cohort of enrolled patients, divided by gender. As shown, arterial hypertension was highly prevalent.

A significant proportion of patients had a history of cardiovascular or metabolic disease, in particular, hypertension (77.4% of the entire cohort), diabetes (27.5%) and coronary heart disease (23.9%).

Table 2 illustrates the characteristics of the patient population according to whether or not they were receiving treatment with statins, including the association with ezetimibe, regardless of their primary or secondary prevention status. A statistically significant difference between the two groups was found regarding total cholesterol, the CIRS indices, history of a previous cardiovascular event, and the proportion of patients receiving five or more drugs. Consistent results were observed when considering any lipid-lowering treatment (see suppl. Table 2, ESM). A separate statistical analysis was performed in the subgroup of patients with no previous history of cardiovascular disease ($n = 908$), in which it was possible to calculate the estimated 10-year risk for fatal events according to the SCORE O.P. function. No significant difference in the SCORE estimate was detected, considering statin treatment (with or without ezetimibe) or any lipid-lowering treatment ($p > 0.1$, data not shown).

Logistic regression analysis was performed in order to better define the individual contribution of variables associated with lipid-lowering treatment. Considering any kind of lipid-lowering therapy as the dependent variable, standard multivariate analysis showed a significant association with female gender, polypharmacy, and the presence of specific cardiovascular conditions such as coronary heart disease and peripheral vascular disease, as outlined in Table 3. A previous diagnosis of dyslipidemia was also, not surprisingly, associated with lipid-lowering treatment

Table 3 Standard logistic regression analysis

Variable	B	SE	Odds ratio	Lower 95% CI	Upper 95% CI	*p* value
Age	−0.027	0.009	0.974	0.958	0.990	0.002*
Gender (male)	−0.252	0.116	0.777	0.619	0.976	0.030*
Systolic blood pressure	0.002	0.003	1.002	0.996	1.009	0.449
Total cholesterol	−0.005	0.001	0.995	0.993	0.998	0.001*
Polypharmacy % (≥5 drugs)	1.151	0.142	3.160	2.393	4.173	<0.001*
Barthel Index	0.004	0.002	1.004	1.000	1.008	0.054
CIRS SI	−0.187	0.431	0.830	0.356	1.930	0.664
CIRS CI	0.022	0.073	1.022	0.886	1.179	0.765
Diabetes	0.142	0.124	1.153	0.904	1.470	0.251
Dyslipidemia	1.191	0.169	3.290	2.362	4.582	<0.001*
Hypertension	0.293	0.155	1.341	0.990	1.816	0.058
Previous CHD event	0.641	0.123	1.898	1.491	2.418	<0.001*
Heart failure	0.268	0.148	1.307	0.978	1.747	0.070
Previous cerebrovascular event	0.253	0.140	1.288	0.980	1.694	0.070
Peripheral vascular disease	0.469	0.154	1.598	1.182	2.159	0.002*
SBT	0.012	0.008	1.012	0.996	1.027	0.132
Constant (β0)	−0.300	0.976	0.741			0.758

Dependent variable: any lipid lowering treatment

CHD coronary heart disease, *CIRS CI* Cumulative Illness Rating Scale, Comorbidity Index, *CIRS SI* Cumulative Illness Rating Scale, Severity Index, *SBT* Short Blessed Test

* Statistically significant ($p < 0.05$)

whereas a negative correlation was detected with age and with total cholesterol.

When only treatment with a statin was taken into consideration (Table 4), similar results were observed regarding age, total cholesterol, polypharmacy, dyslipidemia, coronary events, and peripheral vascular disease.

With both models, no correlation was found with other variables, such as the Comorbidity CIRS Indices and diabetes. A significant correlation was detected with the Barthel Index when considering statin treatment. The possible impact of cardiovascular risk estimate according to the SCORE O.P. function was evaluated with this statistical approach too, in the subgroup of patients in primary prevention. The risk estimate was not significantly associated with either hypolipidemic or statin treatment (data not shown).

Logistic analysis was also repeated in the subgroup of patients (1675) who did undergo cognitive evaluation by the SBT; the SBT score was positively associated [odds ratio (OR) 1.021, CI 1.001–1.041; $p = 0.039$] with any lipid-lowering prescription whereas the trend of the other associations did not change substantially, remaining significant for coronary and peripheral disease, polypharmacy, and, negatively, with serum cholesterol and age (data not shown). When statin prescription (including the association with ezetimibe) was considered, a similar significant association was observed (OR 1.027, CI 1.007–1.048; $p = 0.009$).

Finally, we looked at the association between statin treatment, as the dependent variable, and the different independent variables using stepwise logistic regression analysis. Once again, the variables significantly associated with statin treatment were polypharmacy, dyslipidemia, previous coronary or peripheral vascular disease, hypertension, and, with a negative correlation, total cholesterol and age (suppl. Table 3, see ESM).

4 Discussion

Multiple drug treatment is a major problem in older people. On the one hand, advancing age is associated with increasing cardiovascular risk. Nonetheless, lipid-lowering drugs and in particular statins, the most widely utilized agents of this category, show considerable potential for side effects and pharmacological interactions. This is partly due to hepatic metabolism, which is largely mediated by the isoenzyme CYP3A4 for most compounds [29] in a context of polypharmacy.

It must be considered that the drug regimen received by patients largely reflects pre-hospitalization treatment. As such, it is more likely to be symptomatic of prescribing habits from general practitioners (family doctors) than from hospital specialists.

Table 4 Standard logistic regression analysis

Variable	B	SE	Odds ratio	Lower 95% CI	Upper 95% CI	*p* value
Age	−0.023	0.009	0.977	0.960	0.994	0.007*
Gender (male)	−0.195	0.119	0.823	0.652	1.038	0.100
Systolic blood pressure	0.003	0.003	1.003	0.997	1.010	0.333
Total cholesterol	−0.004	0.001	0.996	0.993	0.998	0.001*
Polypharmacy % (≥5 drugs)	1.129	0.146	3.092	2.321	4.121	<0.001*
Barthel Index	0.005	0.002	1.005	1.000	1.009	0.039*
CIRS SI	−0.147	0.440	0.863	0.364	2.047	0.739
CIRS CI	0.023	0.074	1.023	0.884	1.184	0.758
Diabetes	0.112	0.127	1.118	0.872	1.434	0.379
Dyslipidemia	1.194	0.170	3.299	2.366	4.599	<0.001*
Hypertension	0.349	0.162	1.417	1.033	1.945	0.0319*
Previous CHD event	0.595	0.126	1.812	1.416	2.319	<0.001*
Heart failure	0.242	0.151	1.274	0.947	1.713	0.109
Previous cerebrovascular event	0.210	0.143	1.234	0.933	1.633	0.141
Peripheral vascular disease	0.471	0.156	1.602	1.180	2.174	0.002*
SBT	0.013	0.008	1.013	0.998	1.029	0.097
Constant (β0)	−0.927	1.000	0.396			0.354

Dependent variable: treatment with statins, including the association with ezetimibe

CHD coronary heart disease, *CIRS CI* Cumulative Illness Rating Scale, Comorbidity Index, *CIRS SI* Cumulative Illness Rating Scale, Severity Index, *SBT* Short Blessed Test

* Statistically significant ($p < 0.05$)

In this sample, no relevant gender-related differences could be detected.

A high prevalence of multimorbidity and polypharmacy was confirmed, along with frequent clinical history of cardiovascular events. This is consistent with the epidemiological pattern of hospitalized patients.

As expected, statins represent the vast majority (more than 90%) of lipid-lowering agents, reflecting extremely limited evidence for non-statin drugs in the literature. The association of statins and omega-3 fatty acids was occasionally observed, whereas no patient received a statin plus fenofibrate, presumably because of a reportedly higher risk of adverse events.

Among statins, the use of atorvastatin and simvastatin was prominent both in primary and secondary prevention. Surprisingly enough, we observed a low rate of utilization of pravastatin, which is so far the only drug with evidence-based use in primary prevention in selected older patients [30]. Likewise, the use of fluvastatin was very uncommon, despite the fact that this compound was reported to display a relatively safer pharmacokinetic profile [16, 20]. Finally, the use of ezetimibe added to statin was also infrequent, even though this regimen proved useful in achieving adequate cholesterol targets with a relatively low dosage of statin in older people [31]. In other words, the choice of a particular lipid-lowering agent seems to be consistent with overall published evidence on hypolipidemic treatment as well as general prescription tendencies, rather than following specific guidelines regarding the older population. It should be emphasized, however, that the simvastatin-based trial Heart Protection Study (HPS), although not specifically designed for old-age patients, included the largest number of patients aged over 65 years [32].

It is our considered opinion that, particularly in primary prevention, the prescription of less frequently used drug regimens presenting favorable safety profiles should be encouraged.

At univariate analysis, patients receiving lipid-lowering treatment had significantly lower cholesterol levels. This can be reasonably considered as a consequence of treatment itself. Treated patients also showed a larger proportion of patients receiving more than five drugs and higher CIRS scores. The latter finding corroborates the view that patients with a higher degree of complexity are more likely to receive hypolipidemic drugs, consistent with the higher prevalence of cardiovascular disease in treated patients. Differences in the prevalence of polypharmacy, considered as the intake of five or more drugs, may be seen from the same perspective.

When using standard multivariate logistic analysis and stepwise analysis, polypharmacy was one of the variables significantly associated with treatment. Other clinical variables with a high degree of association with lipid-lowering drug use included a positive history for

cardiovascular conditions such as coronary heart disease and peripheral vascular disease. Previous cerebrovascular events showed a lesser degree of association. The association between statin use and Barthel Index may reflect the impact of these conditions on functional status.

The present data reinforce a trend toward prescription in secondary prevention, in line with national and international recommendations [33–35], even though the number of patients receiving treatment is probably suboptimal. Regarding primary prevention, our data on cardiovascular risk estimate fail to show an association. This might be due to a rather limited sample size, but it could also reflect a limited propensity to utilize risk functions for treatment choice in this age category.

On the other hand, it came as a mild surprise that the presence of diabetes was not associated with the likelihood of receiving hypolipidemic treatment. Indeed, compelling evidence including local and international guidelines [34–36] suggests that diabetes is considered as an equivalent of coronary heart disease. Conversely, this view might represent an oversimplification, and solid evidence encourages the adoption of specific tools taking into account variables reflecting the severity of the disease and the degree of metabolic control [37, 38]. A possible interpretation of our results might be that the choice of prescription is likely to be influenced by the general risk status and metabolic compensation of the patient, rather than by previous diagnoses of diabetes per se.

At logistic analysis, age showed an inverse correlation with the likelihood of receiving lipid-lowering treatment, which was independent of the other variables studied. This finding, which appears to conflict with the data on polypharmacy, might reflect caution toward a potentially dangerous treatment from the point of view of general practitioners. This prescription behavior is sometimes referred to as an 'ageism' bias [20], reiterating the view that older people are often denied appropriate treatment on the basis of age only. Indeed this may hold true in some situations, but on many occasions it is likely to simply represent the result of careful cost-benefit analysis in terms of patients' global benefit, with a view to limited life expectancy as well. As geriatricians are well aware, the most appropriate management for individual patients often implies refraining from adding new drugs in an already overtreated old-age subject. In addition, the benefits of statin treatment on clinical outcomes seem to be reduced in populations where non-cardiovascular mortality risk is higher [39]. In fact, recent reports have reached conflicting conclusions in this field [40–43], while the usefulness of statins with ongoing age has been openly questioned [40, 41].

No stringent guidelines regarding older people are available in the literature. The most recent position papers issued by the American and European Societies of Cardiology [34, 35] only provide generic treatment suggestions and do not address the issue of pharmacotherapy in very old age strata. In general, however, treatment in secondary prevention is encouraged and the prescription behavior described in the present paper is consistent, at least in part, with this view.

At the present time, no guideline takes into consideration the relevance of age-specific conditions, such as multimorbidity and frailty. The evaluation of the functional status of patients [43, 44], and the interaction with their anagraphic age [45], must necessarily lead to the most appropriate choice, which can hardly be standardized and needs to be tailored to the individual patient.

Finally, the results from the subpopulation where a cognitive test could be performed seem to endorse the view that treated patients tend to have a worse performance status, which is independent of the other studied variables. Such a correlation might suggest a detrimental effect of lipid-lowering treatment, on the one hand. On the other, it might indicate that patients with less preserved cognitive functions are more likely to receive a prescription, consistent with the above-mentioned observation on multimorbidity. Once again, the relationship between cognitive function and cholesterol is extremely controversial [46, 47] and would certainly benefit from additional insights.

The analysis of 'real-life' data in a large population of patients with a high degree of complexity, who are systematically excluded from clinical trials, represents a major strength of the present work. Among its limitations, the observational nature of the findings should be mentioned, alongside the consideration that the associations described do not necessarily reflect a case-to-effect relationship, as can be ascertained only with specifically designed trials.

5 Conclusions

This study suggests that the prescription of lipid-lowering agents to older people is strongly influenced by the personal cardiovascular history of patients, rather than other factors. Notwithstanding its limits, a trend towards statin use in secondary prevention has emerged consistently with suggestions and statements derived from international guidelines, although such a prescribing habit might be further encouraged. Advancing age seems to negatively influence the prescribing attitude, whereas polypharmacy seems not to, as it might be perceived to be related to clinical history itself. A specific ad hoc approach, designed for older patients, is obviously needed. Regardless of the aforementioned limitations, however, this study provides a

useful and reliable picture of statin prescription behavior in a real-life setting, in the light of limited evidence in the literature at the present time.

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Compliance with ethical standards

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