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CURRENT OPINION

How Common is Statin Use in the Oldest Old?

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Abstract
There is a lack of evidence surrounding the efficacy of statins in the oldest old (≥ 80 years of age). As such, there is controversy surrounding use of statins in this population. We sought to evaluate the prevalence of statin use in the oldest old worldwide to understand the scope of this issue. We searched PubMed and grey literature over the last 5 years. Studies had to report the prevalence of statin use in adults ≥ 80 years of age. The first author performed screening and extracted data. Our search produced 1870 hits; 14 articles were considered eligible. We found three studies of nursing home residents, eight studies of community-dwelling patients and three studies in the combined population (i.e., both community-dwelling patients and nursing home residents). The prevalence of statin use ranged from 17 to 39% in nursing home residents, 12 to 59% for community-dwelling patients and 18 to 45% in combined populations. Beyond age 80 years, the prevalence of statin use appeared to decrease with advancing age. Statin use was more common as secondary prevention compared with primary prevention. The prevalence of statin use in the oldest old has increased over recent decades. The increase in prevalence appears to be more pronounced in the oldest old compared with younger old, as reported by two studies. Statins are widely used in the oldest old despite the lack of evidence in this population. Given how common statin use is in the oldest old, clinical evidence surrounding their efficacy in this group is urgently needed to guide appropriate use and shared decision-making.

Key Points

There is a lack of evidence to guide statin use in the oldest old.

Statins are commonly used in the oldest old for both primary and secondary prevention across care settings.

Given how common statin use is in this population, clinical evidence to guide appropriate use is urgently needed.

1 Introduction

Statins (HMG-CoA reductase inhibitors) are used to reduce risk of cardiovascular disease (CVD). Their efficacy is established in secondary prevention of CVD and in primary prevention of CVD for high-risk individuals [1–4]. Clinical trials have demonstrated benefit in those aged 40–75 years, but persons ≥ 80 years of age (the oldest old) have been excluded or poorly represented in these trials [5, 6]. Thus, there is limited evidence in this population [5, 6]. The PROSPER trial (Pravastatin in Elderly Individuals at Risk of Vascular Disease; published in 2002) evaluated the efficacy of pravastatin in persons aged 70–82 years (mean age 75 years), showing a reduced risk of coronary heart disease for secondary prevention but not primary prevention [7]. A more recent sub-group analysis of the ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) lipid-lowering trial found no benefit for pravastatin in primary prevention in those aged 75 years or older [8], while a re-analysis of SPRINT (Systolic Blood Pressure Intervention Trial) data (mean age 77 years) likewise found that statins were not beneficial for primary prevention [9]. Finally, the CORONA trial (Controlled Rosuvastatin Multinational Trial in Heart Failure; mean age 73 years, 41% ≥ 75 years of age) found no

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benefit of rosuvastatin over placebo, though this trial was conducted exclusively in patients with heart failure [10]. Given limited evidence, clinicians may rely on data from younger old persons. However, it is unclear whether this evidence can be applied in the oldest old—especially since many of these persons are frail with multiple co-morbidities.

Much attention has been paid recently to the lack of clinical evidence surrounding statin use in the oldest old, particularly in primary prevention [6, 11, 12]. We wanted to better understand the context and scope of this issue and examine how common statin use is in this population.

2 Literature Search Strategy

We searched PubMed on December 11, 2017 (and updated the search on June 6, 2018) using the following search strategies: (a) ((((statin*[Title/Abstract]) OR statins, hmg coa[MeSH Terms])) AND prevalence[Title/Abstract]) AND ((elderly[Title/Abstract]) OR elderly[MeSH Terms]) as well as (b) (statin[Title/Abstract] OR "hydroxymethylglutaryl-coa reductase inhibitors"[MeSH Terms]) AND "aged, 80 and over"[MeSH Terms] (limited to the last 5 years). We further conducted a grey literature search using Google, Google Scholar, and UpToDate and scanned the bibliographies of eligible articles. Articles reporting the prevalence of statin use in persons ≥ 80 years of age were eligible. There was no limit on publication type but only articles published in English were included. One reviewer (WT) scanned all titles and abstracts against eligibility criteria. If an abstract was relevant, the full text of the article was reviewed. One author (WT) confirmed eligibility and extracted data. Data were interpreted and analyzed by the entire author group. If statin use prevalence was reported in different age groups, we only extracted data for age groups ≥ 80 years of age.

3 Available Evidence

Our literature search produced 1870 titles and abstracts. Nineteen full text articles were retrieved and 14 articles were deemed eligible for inclusion (see electronic supplementary material for flow diagram) [13–26]. We found three studies of residents in nursing homes [13, 14, 24], eight studies of outpatients/community-dwelling older persons [15–20, 25, 26] and three studies in the general population (i.e., both outpatients/community-dwelling patients and nursing home residents included in data) [21–23]. The characteristics of the eligible studies and prevalence of statin use are summarized in Table 1. In the nursing home population, the prevalence of statin use ranged from 16.6 to 38.5%. For community-dwelling older persons, eligible studies reported a range between 13.2 and 58.5%. In the general (combined) population, the prevalence ranged from 18 to 45.4%.

Three studies [14, 15, 20] measured prevalence of statin use across different age ranges above age 80 years and found that statin use was less common with increasing age (see Table 1). Two additional studies investigated the influence of age on statin use. Tija et al. found that older age reduced the odds that a patient was receiving a statin (OR 0.97; 95% CI 0.96–0.98 per year) [24], while Taipale et al. found that persons with Alzheimer's disease (AD) age ≥ 90 years were less likely to receive a statin compared with those < 90 years of age with AD (OR 0.28; 95% CI 0.25–0.31) [17]. Statin use also varied according to clinical factors and country, as outlined in Sect. 4.

4 Statin Use in Older Individuals

Based on our literature search, statin use is common and increasing in the oldest old. Differences exist between countries, practice settings, and age groups and based on other clinical factors.

4.1 Different Age Groups

The prevalence of statin use was lower with advancing age [13, 15, 17, 20, 23, 24]. For example, Gulliford et al. found prevalence declined in each higher strata [20]. This may be explained by increasing rates of statin discontinuation with age, which in the Gulliford study increased from 4% per year for ages 80–84 years to 13% for ages 95–99 years) [20]. This finding is supported by Noaman et al., who found that being an octogenarian alone increased the likelihood of having a statin discontinued [26]. Gnjidic et al. also reported that statin discontinuation rates were higher in those aged ≥ 90 years compared with those younger than 90 years [14]. Unfortunately, these studies did not examine the reason or motivation for discontinuation. It is possible that advancing age alone was seen as a potential reason for discontinuation of statins, though it is likely that multiple factors influence this decision. For example, Noaman et al. also found that lack of functional improvement during hospitalization (measured by Functional Independence Measure) also independently predicted statin discontinuation [26]. A recent survey in Finnish male octogenarians suggests that statins should not be discontinued based on age alone as they did not appear to negatively affect quality of life in respondents [27]. However, this survey included relatively healthy men and may not apply to those who are frail and have functional limitations. Another explanation for lower rates of use with advancing age may be that statins are less likely to be initiated. Two studies reported a decline in statin inception with age [20, 23]. Physicians may view lipid-lowering therapy as

Table 1 Study characteristics and prevalence of statin use

Setting	First author, year, country	Study design	Sample size	Age (years)	Population	Prevalence (%)	Comments
Nursing home	Campitelli, 2017, Canada [13]	Cross-sectional	$n=40,891$	≥86	Primary and secondary prevention together	27.6	Prevalence 40% for 76–85 years of age; statin use more likely with polypharmacy (>5 medications) and less likely with increasing frailty and female sex; patients with history of MI or stroke significantly more likely to be using statins
	Gnjidic, 2015, Australia [14]	Prospective cohort over 1 year	$n=288$ $n=152$	80–89 ≥90		38.5 17.8	Statin use associated with polypharmacy and higher co-morbidity index; more common for secondary versus primary prevention (in entire population of statin users age ≥ 70 years, 6% primary prevention and 94% secondary prevention)
	Tija, 2014, USA [24]	Retrospective cohort	$n=10,212$	Mean 85 (SD 7.3)		16.6	Patients with advanced dementia; statin use more likely with diabetes, stroke, hypertension, increasing number of medications, and less likely with increasing age
Outpatient/community-dwelling	Chokshi, 2012, USA [15]	Cross-sectional study (over 5 years)	$n=22,646$	80–84	Primary	26	Prevalence 24% overall in ages ≥ 80 years; patients with higher co-morbidity index, dementia less likely to be taking statins
					Secondary	35	
				85–89	Primary	21	
					Secondary	28	
				≥90	Primary	12	
					Secondary	19	
	Johansen, 2015, USA [16]	Longitudinal survey	$n=13,099$	≥80	Primary	34.1	
					Secondary	52[a]	
	Taipale, 2016, Finland [17]	Longitudinal registry-based study	$n=3319$ $n=3319$	≥90 ≥90	Primary and secondary	15.3 with AD 13.2 without AD	Persons aged ≥ 90 years of age were less likely to be using statins compared with those aged < 90 years
	Upmeier, 2013, Finland [18]	Longitudinal registry-based study	$n=833,051$ (age 70+)	≥80	Primary and secondary	34[a] men 31[a] women	Prevalence of statin use increased with increasing CVD risk (in entire population of statin users aged ≥ 70 years, 61% had high CVD risk, 7% low CVD risk, moderate risk not reported)

Table 1 (continued)

Setting	First author, year, country	Study design	Sample size	Age (years)	Population	Prevalence (%)	Comments
	Turner, 2014, Australia [19]	Cross-sectional study	$n=106$	≥80	Primary	18.9	Geriatric oncology clinic
					Secondary	19.8	
	Noaman, 2018, Australia [26]	Retrospective chart review	$n=423$	≥80	Primary and secondary	43	Patients admitted to geriatric internal medicine unit; statin use more common in secondary prevention (in total population of statin users, 70% using for secondary versus 30% for primary) and in those with CVD risk factors; less common in persons with dementia
	Chee, 2018, Australia [25]	Retrospective chart review	$n=852$	≥80	Primary	10.0	Prevalence 42% overall; patients admitted to internal medicine unit; additional 5.5% taking statins with unspecified indication
					Secondary	26.5	
	Gulliford, 2017, UK [20]	Population-based cohort study	$n=23,060$	80–84	Primary and secondary	58.5	Prevalence 49% overall in those aged ≥80 years; 19% primary prevention and 30% for secondary prevention Statin use more common with increasing frailty
			$n=18,981$	85–89		53.2	
			$n=14,724$	90–94		42.3	
			$n=6905$	95–99		26.6	
			$n=726$	≥100		12.0	
General population (community-dwelling and nursing home)	Jacobs, 2013, Israel [21]	Longitudinal cohort study	$n=702$	85	Primary and secondary	45.4	No information on indication
	Proulx, 2015, Canada [22]	Cross-sectional study	Not reported	≥85		39.1	Data from public drug programs; no information on indication

AD Alzheimer's disease, *CVD* cardiovascular disease, *SD* standard deviation, *UK* United Kingdom, *USA* United States of America

[a]Read from plot

unnecessary in patients with limited life expectancy (e.g., advanced dementia) [28]; however, the attitudes towards statin prescribing in the oldest old who are not at end of life have not been examined.

4.2 Trends in Statin Use

The prevalence of statin use in the oldest old has increased in past decades [16, 18, 20, 23]. Gulliford et al. reported that 9% of women and 12% of men aged 80 years and older were prescribed statins in 2005 compared with 46% of women and 55% of men in 2015 [20]. Upmeier et al. similarly reported a 5- to 6-fold increase in the prevalence of statin use from 2000 to 2008 [18]. They investigated change in prevalence of statin use in different age groups over age 70 years. While statin use was more likely with higher CVD risk overall, these authors found that the highest increase in prevalence of statin use was in low-risk persons 80 years and older, though statin use was still low overall in this sub-population. Wallach-Kildemoes et al. evaluated the change in different age groups and reported that the largest increase in prevalence of statin use between 2000 and 2010 was in those aged 75 years and older [23].

The increasing proportion of persons over 80 using statins is suggested to be due to a 'cohort effect' (i.e., patients being started on statins in their 60s and 70s, aging, and continuing on statins into their 80s or 90s) [20, 23]. The cohort effect is likely due to increased prescribing of statins beginning in the 2000s in response to mounting evidence of benefit in those at high risk of CVD (and subsequent recommendations from major society guidelines). Indeed, increasing use of statins has contributed greatly to treatment and prevention of CVD. Unfortunately, there remains a lack of evidence regarding long-term use (e.g., $\geq$ 10 years) [6]. The potential benefit of statin treatment initiated appropriately at age 60 years and continued into the 80s or 90s is unclear [6]. However, the population who began to use statins in their 60s and continued on them appears to represent a large proportion of prevalent statin users aged $\geq$ 80 years. Long-term statin users aged > 80 years can represent a clinical challenge. While major cardiovascular societies have incorporated consideration of those 75 years of age or older into guidelines [29], there remains little evidence to guide decision making. Contemporary guidance suggests continuing statin use in those 75 years of age or older with clinical CVD based on limited data [29, 30].

The broadening of populations recommended to take statins (e.g., statins for primary prevention in those at low risk of CVD, or treating high cholesterol alone versus overall CVD risk) has also been suggested to contribute to increases in statin use in the oldest old [23]. Statin use in individuals at low risk of CVD for primary prevention has been questioned [31]. Current guidelines acknowledge the lack of evidence surrounding statin use for primary prevention in the oldest old and recommend 'individualizing' treatment in the primary prevention population aged 75 years and older [29].

4.3 Factors Associated with Statin Use in the Oldest Old

The prevalence of statin use among the oldest old was higher in secondary prevention compared with primary prevention. This was consistent across studies that separated results by indication for use (see Table 1). This finding is not surprising given stronger evidence of benefit for secondary versus primary prevention. Statins are more likely to be initiated or continued for secondary prevention [20, 26], which explains the higher prevalence in the secondary prevention population. It also appears that statins are less likely to be discontinued if being used for secondary prevention, which may also explain the higher rate of use for secondary prevention versus primary prevention [20, 26]. Prevalent statin use was slightly more common in males compared with females, as reported by several studies [13, 16, 18, 20, 23, 24]. The slightly higher prevalence of statin use in men reported by most studies may be explained by the greater risk of developing CVD in men (particularly if men are 'cohort' users continuing on statins from a younger age) [32]. Wallach-Kildemoes et al. found no sex differences in incident statin use beyond age 60 years [23]. They offer that the similar incidence may be due to statins being prescribed based on cholesterol level alone versus overall CVD risk in primary prevention.

In the outpatient population, Chokshi et al. reported that a higher co-morbidity index was associated with a lower chance of receiving a statin [15]. This is in line with the findings of Noaman et al., who reported that a higher co-morbidity index increased the likelihood of receiving a statin [26]. In contrast, Gnjidic et al. found that those with a higher co-morbidity index were more likely to receive a statin in a nursing home population [14]. Further, Tija et al. studied the advanced dementia population living in a nursing home and reported that statin use was more likely in patients with co-morbidities such as hypertension, diabetes mellitus, or stroke [24]. These findings suggest that the presence of multiple co-morbidities decreases the likelihood of receiving a statin in the community but increases the likelihood in persons living in nursing homes. One explanation for the discrepancy is that in the Gnjidic et al. study, 94% of statin users were receiving statins for secondary prevention at baseline [14]. Thus, even with more co-morbidities, the validity of statin use may be perceived to be greater and people would be kept on statins.

There were consistent findings on the association between increasing medication use and statins. All three studies in nursing home residents found that polypharmacy ($\geq$ 5

medications) or increasing numbers of medications was associated with an increased likelihood of receiving a statin [13, 14, 24]. Discordant findings were found regarding frailty. Gulliford et al. found that statin use in an outpatient population was more common with increasing frailty (prevalence in severe frailty was 69 vs 26% in fit patients) [20]. Conversely, Campitelli et al. reported that statin use was less likely with increasing frailty in the nursing home population [13, 20]. This is consistent with a prospective cohort study conducted in a nursing home which also reported that the prevalence of statin use decreased with increasing frailty [33]. The discrepancy in the effect of frailty on statin use may be explained by differences in the frailty indices used and the populations studied. Gulliford et al. categorized patients as mildly, moderately, or severely frail using an index based on primary care data [20, 34]. However, the studies conducted in nursing homes used indices specific for the nursing home population [13, 35]. The characteristics incorporated into each of these indices differed, which may explain the difference in findings. The differences in the populations could also be a factor. People living in nursing homes may be frailer on average compared with those living in the community. Thus, the relative effect of increasing frailty in the nursing home population may be different than the effect in a community-dwelling population.

4.4 Differences in Statin Use across Countries

Comparing the prevalence of statin use across countries is challenging as data was collected at different time points and populations differed across studies. Differences in statin use may also be explained partly by factors outlined above. However, it is possible to make general comparisons across different countries.

In outpatients (see Table 1), statin use appeared to be comparable in the USA, Australia and Finland, but may be higher in the UK. Statin use in Israel and Canada was comparable in the general population; however, Denmark had a lower prevalence of use. In the nursing home population, Canada and Australia reported similar rates of statin use. The prevalence reported by Tija et al. in the US was lower [24]. However, Tija et al. only included patients with advanced dementia, which may explain the lower rate as increasing frailty and dementia have both been associated with reduced likelihood of receiving a statin in nursing home patients [13, 24].

The variation in statin use between comparable populations indicates that the oldest old do not necessarily receive similar treatment. Differences may be explained by variations in clinical guidelines between countries, particularly in recommendations for use of statins in the oldest old, which are primarily based on expert opinion [23, 29]. In some countries, the threshold for initiating statins in the primary prevention population has been lower, which may also explain the differences in rates of use [23]. However, the differences between guidelines still do not clarify which group(s) received appropriate treatment given the lack of evidence.

4.5 Limitations

We did not use a systematic search to identify eligible articles, though we did conduct a thorough search of PubMed (scanning 1870 titles) and grey literature. It possible we did not identify all articles reporting rates of statin use in the oldest old. Another limitation is that studies reported statin use at different time points and used different age ranges, sample sizes, and populations. This made it challenging to draw comparisons across studies in some cases. The level of detail provided in the studies also differed. For example, the indication for statin use was not always reported, which also made it difficult to compare across studies.

5 Conclusions

Statin use is common in the oldest old in both community-dwelling and nursing home patients in Western countries. However, there is limited evidence on the efficacy of statins in the oldest old, particularly for primary prevention and with long-term use beyond age 80 years. It is important that policy makers, researchers, and clinicians are aware of the scope of this issue. Our findings underscore that high-quality evidence surrounding the benefits and harms of statins in the oldest old is urgently needed to guide appropriate use. Decisions surrounding statin use in this population should be individualized and are likely to be dependent on patient values and preferences. Thus, our findings also underscore the importance of engaging older statin users in discussions surrounding statin use to arrive at shared decisions consistent with patient values and preferences. Given how common statin use is in this population, tools or frameworks that facilitate discussions of statin use in the oldest old would likely be helpful in clinical practice.

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Compliance with Ethical Standards

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