

SHORT REPORT

Statin use and discontinuation in Danes age 70 and older: a nationwide drug utilisation study

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Abstract

Background and objective: There is limited evidence on the clinical effects of statins in older persons. We aimed to explore statin use and discontinuation patterns in Danes age 70 and older.

Design: Register-based drug utilisation study.

Setting: Danish nationwide health registries.

Subjects: All Danish persons aged ≥ 70 years between 2011 and 2016.

Measurements: (1) Monthly prevalence and (2) quarterly incidence of statin use, (3) characteristics of new users, (4) total amount of statin redeemed, (5) statin discontinuation rate between 2014 and 2016 in long-term statin users and (6) factors associated with discontinuation.

Results: We identified 395,279 unique older statin users between 2011 and 2016. The prevalence increased from 30% in 2011 to 33% in 2016 (23% for primary prevention and 56% for secondary prevention in 2016). The quarterly incidence fell from 11 per 1,000 persons in 2011 to 7 per 1,000 persons in 2016. The prevalence was generally stable in those 70 to 79 years. In those aged ≥ 80 years, the prevalence increased despite decreasing incidence. The proportion of persons initiating for primary prevention decreased from 58% in 2011 to 52% in 2016. Approximately 19% of long-term statin users discontinued therapy between 2014 and 2016. Increasing age was the strongest predictor of statin discontinuation.

Conclusions: Approximately one in three Danes age ≥ 70 years were taking statins in 2016. The characteristics of incident users shifted between 2011 and 2016, with less people age 80 and older starting on statins and fewer people starting for primary prevention.

Keywords: statins, drug utilisation, medication discontinuation, older people

Key points

- Around one in three Danes 70 years and older were taking statins in 2016.
- From 2011 to 2016, prevalence increased slightly while incidence decreased.
- The characteristics of incident statin users shifted, with less initiation for primary prevention and in those 80+ years old.
- Around one in five long-term statin users discontinued therapy from 2014 to 2016.

Introduction

Statin use is used to reduce risk of cardiovascular disease, both in those with a history of cardiovascular disease (secondary prevention) and those without (primary prevention).

Limitations in the statin evidence base have been highlighted for older persons [1,2]. In particular, evidence of benefit is conflicting for initiation in primary prevention, and there is little evidence among those who are frail or have multiple co-morbidities [2–5]. Contemporary guidance advocates an

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individualised approach to statin use and discontinuation among older persons [6–8]. The aim of our study was to examine patterns of statin use, initiation and discontinuation, as well as factors associated with discontinuation in older Danes.

Methods

We described measures of statin use and discontinuation in older persons (≥ 70 years of age) in Denmark from 2011 to 2016.

Data sources

Data were obtained from the Danish National Prescription Registry [9], Danish National Patient Register [10], Population Education Register [11], Danish Civil Registration System [12] and Danish Register of Causes of Death [13]. Codes and definitions are provided in [Supplementary Table S1](#).

Research questions

Extent of statin use

The total annual statin use was calculated as the total number of defined daily doses (DDD) of all statins redeemed each year from the Danish National Prescription Registry.

Prevalence of use

We determined the proportion of statin use per 100 persons on the first of each month. Prevalence was determined overall, in 5-year age categories, by sex and by indication (primary or secondary prevention). We identified secondary prevention using ICD-10 codes for cardiovascular disease (myocardial infarction, angina, ischemic heart disease, peripheral arterial disease and ischemic stroke or transient ischemic attack), while primary prevention users were free of cardiovascular disease. Statin use on the first of each month was defined based on the days' supply of a prescription plus 20%.

Incidence of statin use

The quarterly incidence of statin use (per 1,000 persons) was calculated overall and according to age, sex and indication categories defined above. The denominator was the population on the first of each quarter who had not filled a statin prescription in the previous five years.

Characteristics of incident statin users

We summarised the following characteristics of incident statin users for each study year: age, sex, indication, comorbidities, Charlson co-morbidity score [14], concomitant

medication use, education, marital status and region of residence. Refer to [Supplementary Tables S1 and S2](#) for further detail.

Rate of discontinuation in long-term statin users

Long-term users were those exposed to statins on 1 January 2014 who filled one or more statin prescriptions each calendar year 2009–2013. We followed these persons until 31 December 2016 and calculated the statin discontinuation rate over this period. Discontinuation was defined as not filling a statin prescription during the days' supply of the previous prescription plus 180 days. We excluded persons who died within 180 days of their last prescription, to exclude those where death (or impending death) was the reason for discontinuation. A 180-day grace period was used to ensure that we captured true discontinuation and based on exploration of prescription patterns (see [Supplementary Table S3](#)).

Factors associated with statin discontinuation among long-term users

We evaluated *a priori* defined factors (see [Supplementary Tables S4 and S5](#)) associated with statin discontinuation in those classified as discontinuers above. We used logistic regression, reporting both crude odds ratios (OR) for each factor and adjusted ORs after incorporating all factors into a single model.

Approvals

Ethics approval was not required. The study was registered at the University of Southern Denmark's inventory (record No. 18/15245).

Results

Extent of statin use

We identified 395,279 unique statin users age 70 or older, filling 6,513,347 prescriptions between 2011 and 2016. Statin use increased from 84 million DDDs in 2011 to 120 million DDDs in 2016 ([Figure 1](#)). Simvastatin was the most commonly used statin, followed by atorvastatin, and then rosuvastatin, with atorvastatin use increasing over time.

Prevalence

The prevalence in the overall population of Danes age 70 or older was relatively stable (30% in 2011 and 33% in 2016; [Figure 2](#)). Similar trends were noted for primary prevention (21% in 2011 and 23% in 2016) and secondary prevention (54 and 56%). Prevalence broken down by 5-year age categories, sex and indication is provided in [Supplementary Figures S1–S4](#). In general, prevalence increased slightly in the age groups 80 years and older and was stable in the age groups between 70 and 79 years.

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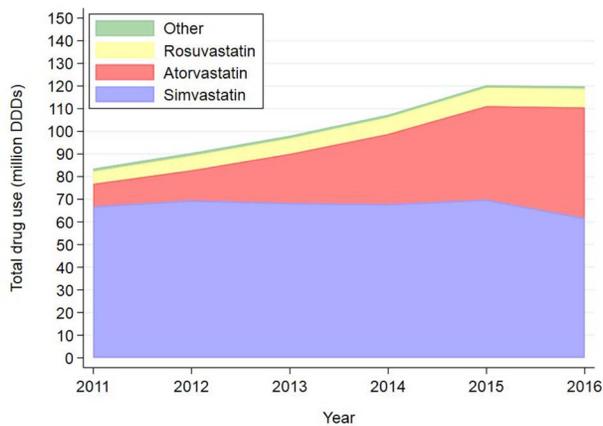


Figure 1. Nationwide extent of statin use for Danes age 70 and older between 2011 and 2016. Other = fluvastatin, pravastatin, lovastatin, simvastatin + ezetimibe, atorvastatin + ezetimibe. Abbreviation: DDD = defined daily dose.

Incidence

The quarterly incidence in the overall population of Danes age 70 or older fell from around 11 per 1,000 persons in early 2011 to around 7 per 1,000 persons in late 2016 (Figure 2). There was a decrease in incidence for primary and secondary prevention (Figure 2). Incidence broken down by age, sex and indication is provided in Supplementary Figures S5–S8.

Characteristics of incident users

Characteristics of incident statin users are presented in Supplementary Table S2. Statin initiators commonly had comorbidities such as type 2 diabetes (11–14%) or hypertension (31–33%). The median Charlson co-morbidity score was 1 (IQR 0 to 2) across the study period, and incident statin users redeemed a median of 6 (IQR 4 to 9) concomitant medications. The proportion of incident users over the age of 80 years dropped from 30% in 2011 to 25% in 2016. The proportion initiating statins for primary prevention decreased from 58% in 2011 to 52% in 2016.

Statin discontinuation in long-term users

On 1 January 2014, there were 169,038 Danes age 70 and older who had taken a statin for 5 years or more (Supplementary Table S4). Approximately 19% discontinued their statin between 2014 and 2016. The odds of discontinuation increased with each increasing 5-year age group (see Supplementary Table S5). The odds of discontinuation also increased with each increasing level of Charlson co-morbidity score (e.g. aOR 1.34, 95% CI 1.26 to 1.43, for a score of 5+ compared to 0). Concomitant cardiovascular medication use was associated with reduced odds of discontinuation, ranging from a 15% reduction (aOR 0.85, 95% CI 0.82 to 0.87) for ACEIs/ARBs to a 22% reduction (aOR 0.78, 95% CI 0.74 to 0.82) for anticoagulants. A diagnosis of MI (aOR 0.91, 95% CI 0.88 to 0.95) or ischemic

stroke (aOR 0.91, 95% CI 0.87 to 0.96) was also associated with reduced odds of discontinuation. A full summary is in Supplementary Table S5.

Discussion

Around one in three Danes age 70 and older were taking statins between 2011 and 2016. Despite a stable prevalence, incident statin use dropped slightly. The proportion of persons over 70 years of age initiating statins for primary prevention fell. Around one in five long-term statin users discontinued therapy between 2014 and 2016. Increasing age was the strongest predictor of discontinuation.

Limitations

We calculated prevalence using a 20% grace period attached to the end of a prescription. It is possible that those with irregular filling patterns were not captured in our prevalence estimate each month. The Danish National Prescription Registry captures medications redeemed at the pharmacy, and thus we do not know whether medications were actually taken by patients. In defining discontinuation, we used a grace period of 180 days to minimise misclassification; however, around 37% of those considered to discontinue statins, restarted therapy (see Supplementary Table S3). Finally, with respect to factors associated with discontinuation, we were only able to investigate (and adjust for) factors which are captured in the Danish registers.

Comparison to existing literature

Our findings on prevalence are consistent with a previous Danish study with data up to 2010 [15]. Studies in other countries have reported prevalence rates of 12–60% in persons 80 years and older [16]. The decreasing incidence we observed is consistent with studies from the UK and Australia [17,18]. We found the rise in prevalence was more pronounced in those 80 and older. This may suggest a “cohort effect” [19] where people started statins at a younger age and have remained on them into their 80s and 90s.

The discontinuation rate we observed in long-term users was slightly lower than what has been reported over the first years following statin initiation [20,21]. The factors we identified to be associated with discontinuation in long-term statin users generally reflect what has been reported in early statin users, with increasing age being the strongest predictor of statin discontinuation [19,21–24]. Similar to a previous study [21] of early discontinuation, we found higher comorbidity scores increased likelihood of discontinuation. It is possible that with increasing co-morbidity, the potential benefit of statins becomes less compelling, prompting discontinuation [25].

Clinical implications and future research

There is limited evidence surrounding statin use among older persons, particularly those age 80 and older and those

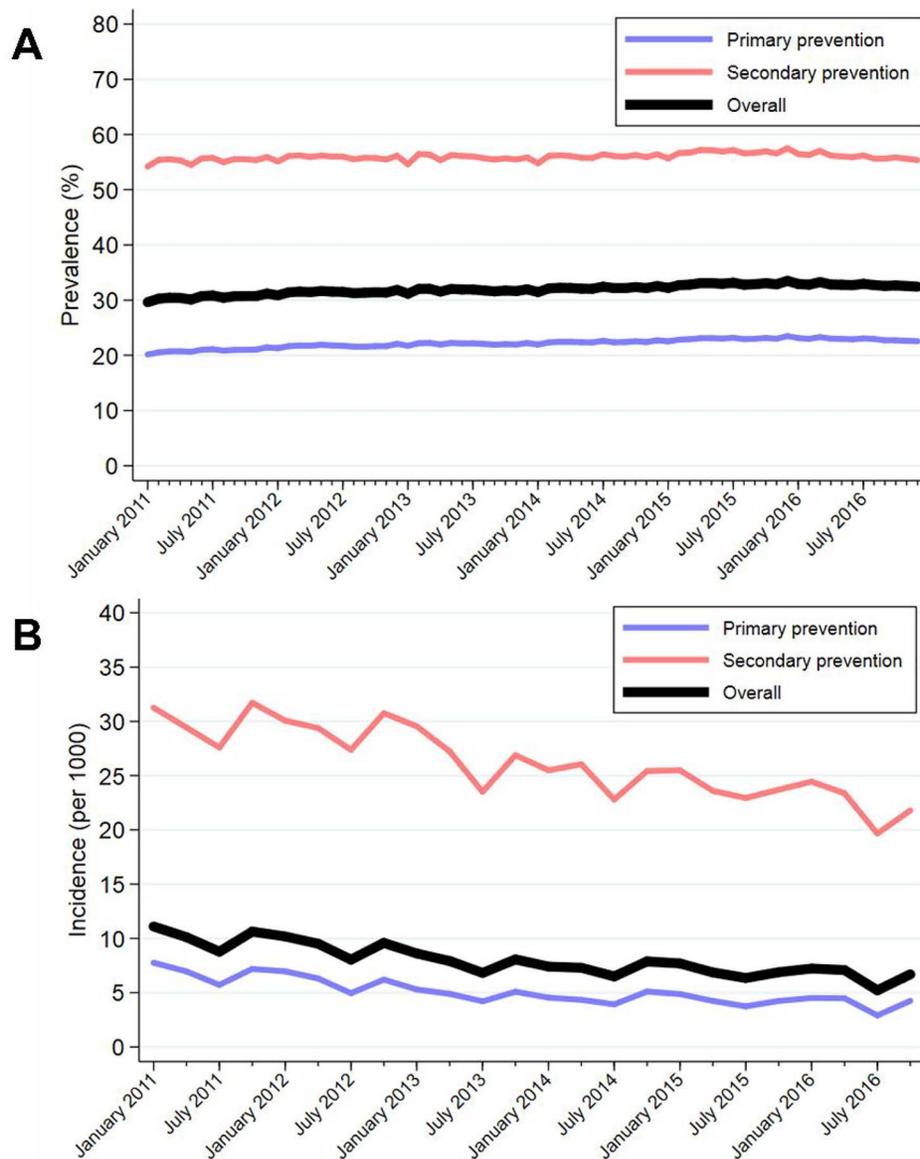


Figure 2. Nationwide prevalence and incidence of statin use in Danes age 70 and older between 2011 and 2016 (A = prevalence, B = incidence).

who are frail, along with limited evidence and guidance on statin discontinuation [6,8,26,27]. Our findings highlight the need for greater understanding around how statin treatment and discontinuation decisions are made in older persons, and the need for guidance and evidence to support these decisions.

Conclusion

Statin use was common in older Danes between 2011 and 2016, though the incidence gradually fell. Approximately, 19% of long-term older statin users discontinued their statin between 2014 and 2016.

Supplementary Data: [Supplementary data](#) mentioned in the text are available to subscribers in *Age and Ageing* online.

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Declaration of Conflicts of Interest: None.

References

1. Strandberg TE, Kolehmainen L, Vuorio A. Evaluation and treatment of older patients with hypercholesterolemia. *JAMA* 2014; 312: 1136.
2. Hawley CE, Roefaro J, Forman DE, Orkaby AR. Statins for primary prevention in those aged 70 years and older: a critical

- review of recent cholesterol guidelines. *Drugs Aging* 2019; 36: 687–99.
3. Armitage J, Baigent C, Barnes E *et al*. Efficacy and safety of statin therapy in older people: a meta-analysis of individual participant data from 28 randomised controlled trials. *Lancet* 2019; 393: 407–15.
 4. Han BH, Sutin D, Williamson JD *et al*. Effect of statin treatment vs usual care on primary cardiovascular prevention among older adults: the ALLHAT-LLT randomized clinical trial. *JAMA Intern Med* 2017; 177: 955–65.
 5. Huesch MD. Association of Baseline Statin use among Older Adults without Clinical Cardiovascular Disease in the SPRINT trial. *JAMA Intern Med* 2018; 178: 560–61.
 6. Krishnaswami A, Steinman MA, Goyal P *et al*. Deprescribing in older adults with cardiovascular disease. *J Am Coll Cardiol* 2019; 73: 2584–95.
 7. van Middelaar T, van Charante EPM. Deprescribing preventive medication in older patients. *Br J Gen Pract* 2018; 68: 456–7.
 8. van der Ploeg MA, Floriani C, Achterberg WP *et al*. Recommendations for (discontinuation of) statin treatment in older adults: review of guidelines. *J Am Geriatr Soc* 2019; 68: 417–25.
 9. Pottegård A, Schmidt SAJ, Wallach-Kildemoes H, Sørensen HT, Hallas J, Schmidt M. Data resource profile: the Danish National Prescription Registry. *Int J Epidemiol* 2017; 46: 798–98f.
 10. Schmidt M, Schmidt SAJ, Sandegaard JL, Ehrenstein V, Pedersen L, Sørensen HT. The Danish National Patient Registry: a review of content, data quality, and research potential. *Clin Epidemiol* 2015; 7: 449–90.
 11. Jensen VM, Rasmussen AW. Danish education registers. *Scand J Public Health* 2011; 39: 91–4.
 12. Schmidt M, Pedersen L, Sørensen HT. The Danish civil registration system as a tool in epidemiology. *Eur J Epidemiol* 2014; 29: 541–9.
 13. Helweg-Larsen K. The Danish register of causes of death. *Scand J Public Health* 2011; 39: 26–9.
 14. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol* 1994; 47: 1245–51.
 15. Wallach-Kildemoes H, Stovring H, Holme Hansen E, Howse K, Pétursson H. Statin prescribing according to gender, age and indication: what about the benefit-risk balance? *J Eval Clin Pract* 2016; 22: 235–46.
 16. Thompson W, Pottegård A, Nielsen JB, Hastrup P, Jarbøl DE. How common is statin use in the oldest old? *Drugs Aging* 2018; 35: 679–86.
 17. O’Keeffe A, Nazareth I, Petersen I. Time trends in the prescription of statins for the primary prevention of cardiovascular disease in the United Kingdom: a cohort study using the health improvement network primary care data. *Clin Epidemiol* 2016; 8: 123–32.
 18. Ofori-Asenso R, Ilomäki J, Zomer E, Curtis AJ, Zoungas S, Liew D. A 10-year trend in statin use among older adults in Australia: an analysis using national pharmacy claims data. *Cardiovasc Drugs Ther* 2018; 32: 265–72.
 19. Gulliford M, Ravindrarajah R, Hamada S, Jackson S, Charlton J. Inception and deprescribing of statins in people aged over 80 years: cohort study. *Age Ageing* 2017; 46: 1001–5.
 20. Ofori-Asenso R, Jakhu A, Zomer E *et al*. Adherence and persistence among statin users aged 65 years and over: a systematic review and meta-analysis. *Journals Gerontol - Ser A Biol Sci Med Sci* 2018; 73: 813–9.
 21. Thompson W, Jarbøl DE, Hastrup P, Nielsen JB, Pottegård A. Statins in older Danes: factors associated with discontinuation over the first 4 years of use. *J Am Geriatr Soc* 2019; 67: 2050–57.
 22. Ofori-Asenso R, Ilomäki J, Tacey M *et al*. Predictors of first-year nonadherence and discontinuation of statins among older adults: a retrospective cohort study. *Br J Clin Pharmacol* 2019; 85: 227–35.
 23. Halava H, Huupponen R, Pentti J, Kivimäki M, Vahtera J. Predictors of first-year statin medication discontinuation: a cohort study. *J Clin Lipidol* 2016; 10: 987–95.
 24. Noaman S, Al-Mukhtar O, Abramovic S *et al*. Changes in statin prescription patterns in patients admitted to an Australian geriatric subacute unit. *Hear Lung Circ* 2019; 28: 423–29.
 25. van der Ploeg MA, Streit S, Achterberg WP *et al*. Patient characteristics and general practitioners’ advice to stop statins in oldest-old patients: a survey study across 30 countries. *J Gen Intern Med* 2019; 34: 1751–57.
 26. Kutner JS, Blatchford PJ, Taylor DH *et al*. Safety and benefit of discontinuing statin therapy in the setting of advanced, life-limiting illness. *JAMA Intern Med* 2015; 175: 691.
 27. Giral P, Neumann A, Weill A, Coste J. Cardiovascular effect of discontinuing statins for primary prevention at the age of 75 years: a nationwide population-based cohort study in France. *Eur Heart J* 2019; 40: 3516–25.

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