Drug use in centenarians compared with nonagenarians and octogenarians in Sweden: a nationwide register-based study

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Abstract

Background: the number of centenarians increases rapidly. Yet, little is known about their health and use of medications.

Objective: to investigate pharmacological drug use in community-dwelling and institutionalised centenarians compared with nonagenarians and octogenarians.

Methods: we analysed data on dispensed drugs for centenarians (n = 1,672), nonagenarians (n = 76,584) and octogenarians

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(\(n = 383,878\)) from the Swedish Prescribed Drug Register, record-linked to the Swedish Social Services Register. Multivariate logistic regression analysis was used to analyse whether age was associated with use of drugs, after adjustment for sex, living situation and co-morbidity.

**Results:** in the adjusted analysis, centenarians were more likely to use analgesics, hypnotics/sedatives and anxiolytics, but less likely to use antidepressants than nonagenarians and octogenarians. Moreover, centenarians were more likely to use high-ceiling diuretics, but less likely to use beta-blockers and ACE-inhibitors.

**Conclusions:** centenarians high use of analgesics, hypnotics/sedatives and anxiolytics either reflects a palliative approach to drug treatment in centenarians or that pain and mental health problems increase into extreme old age. Also, centenarians do not seem to be prescribed cardiovascular drug therapy according to guidelines to the same extent as nonagenarians and octogenarians. Whether this reflects an age or cohort effect should be evaluated in longitudinal studies.

**Keywords:** centenarians, drugs, elderly, pharmacoepidemiology, register-based research

**Introduction**

The world has seen dramatic reductions in old age mortality [1]. Life expectancy has increased and the number of centenarians has doubled or more in most developed countries during the last 10 years [2]. It has been estimated that if life expectancy continues to rise at the same rate as during the last 160 years, about 50% of people born in the beginning of this century will live to see their 100th birthday [3]. Thus, extremely old people should be regularly included in epidemiological studies, and not only in highly specialised centenarian studies, which often focus on centenarians as healthy survivors [4–6]. On the contrary, centenarians are not necessarily healthy when they reach one hundred years [7]. Rather, morbidity and mortality have been postponed into extreme old age [8–10].

Drug therapy in old age is complicated by multiple diseases, organ failure and cognitive impairment. Older people are therefore more sensitive to drugs and at the same time they use more drugs than younger age groups. Taken together, elderly people have the greatest risk of adverse drug reactions [11]. In contrast to the common notion that drug use increases with higher age, previous studies have indicated that drug use is lower in centenarians than in nonagenarians [6, 12, 13]. However, research on drug use in centenarians is scarce and often based on small and selected samples without comparisons with other age groups [7, 14–16]. Thus, we used nationwide register data to investigate drug use in both community-dwelling and institutionalised centenarians compared with nonagenarians and octogenarians. To our knowledge, this study is the largest investigation of drug use in centenarians published so far.

**Methods**

**Study population**

The Swedish Prescribed Drug Register is one of the largest pharmacoepidemiological databases in the world. Data are collected at Swedish pharmacies and then transferred to the

National Board of Health and Welfare. The register contains individual-based information on all prescribed dispensed drugs in Sweden (about nine million inhabitants). Over-the-counter drugs, drugs used in hospitals or drugs supplied from drug storerooms are not covered in the register. Variables include detailed data on dispensed drugs, age, sex, personal identification number and place of residence [17].

We focused on individuals born 1908 or earlier, who were dispensed a prescribed drug between 1 July and 30 September 2008 (\(n = 1,672\)). This population of centenarians corresponded to 94% (1,672/1,775) of the total population aged 100 years and older in Sweden on 30 September 2008 according to Statistics Sweden’s census data. For age-related comparisons of drug use, we also included people born 1909–28 (\(n = 460,462\)).

Information from the 3-month period about when the prescription was filled, the amount of drug and the prescribed dosage was used to calculate the duration of drug exposure to obtain a list of concurrently used drugs on the last day of the study period. Thus, drug use was evaluated for each individual on the arbitrarily chosen date of 30 September 2008. In Sweden, the maximum quantity of drugs prescribed is for 90-day supply [18, 19]. When prescribed dosage was incomplete or missing (8.7%), we based our calculations of drug exposure on defined daily doses (DDDs). The DDD is the assumed average dose per day for a drug used for its main indication in adults [20]. For each drug, the mean prescribed daily dose (PDD) [20] for regular use was calculated. In the few cases where the PDD could not be calculated, we assumed 0.9 DDDs for regularly used drugs (based on calculations of the total mean value for regularly used drugs among the elderly in the study population). For drugs prescribed as needed, 0.45 DDDs (50% of 0.9) was employed. For dermatological and eye preparations, 1 DDD was assumed [19]. If a person was dispensed the same drug in different doses during the study period, this was counted as one dispensed drug.

The study population derived from the Swedish Prescribed Drug Register was record-linked by personal
identification number to the Swedish Social Services Register to obtain information about living situation (i.e. community-dwelling or institution) on 30 June 2008. The Swedish Social Services Register has national coverage of individual-based information about social services financed by Swedish municipalities, including institutional care for people aged 65 years and older. In Sweden, only a negligible amount of institutional care for older people falls outside the municipal system and very few persons receive long-term care in hospitals.

**Measurements**

The dispensed drugs were classified according to the Anatomical Therapeutic and Chemical classification system (ATC), as recommended by the World Health Organization [20].

Age was categorised into three groups: 80–89 (octogenarians; reference group), 90–99 (nonagenarians) and >100 years (centenarians). Living situation was defined as community-dwelling (own home) or institution (e.g. nursing home, sheltered accommodation). Number of other drugs, used as a proxy for overall co-morbidity [21], consisted of the number of filled prescriptions other than the drugs under study.

**Statistical analysis**

The most commonly dispensed drug classes in centenarians were compared with nonagenarians and octogenarians. We used both univariate and multivariate logistic regression analysis to investigate whether age was related to use of these drugs. In the univariate (unadjusted) analyses, only age was entered as explanatory variable, without adjustment for other variables. In the multivariate (adjusted) analyses, adjustment was made for sex, living situation and number of other drugs. The results are expressed as odds ratios (ORs) with 95% confidence intervals (CIs). SPSS for Windows (SPSS, Version 17, Chicago, IL, USA) was used for the analyses.

**Results**

On average, centenarians were 101 years old and used 5.1 drugs per person, nonagenarians were 92 years old and used 5.7 drugs and octogenarians were 84 years and used 5.3 drugs. Table 1 shows that institutionalised used on average more drugs than community-dwelling persons, although this difference was smaller for centenarians. The majority of the study participants were women and the proportion of women increased with age (octogenarians: 62%; nonagenarians: 72% and centenarians: 84% women). The proportion of institutionalised people also increased with age (octogenarians: 11%; nonagenarians: 34% and centenarians: 59% in institutions) and women lived in institutions to a greater extent than men in all three age groups.

Table 2 shows 16 of the most commonly dispensed drugs classes among centenarians compared with nonagenarians and octogenarians stratified by living situation. Institutionalised individuals had a higher prevalence of use of most drug classes compared with their community-dwelling counterparts. However, this difference was in general less pronounced in centenarians.

The most frequently used drug class in centenarians was high-ceiling diuretics, which was less common in nonagenarians and octogenarians. However, other types of cardiovascular drugs (i.e. antithrombotic agents, beta-blockers and ACE-inhibitors) were less common in centenarians compared with nonagenarians and octogenarians.

The second most commonly used drug class among centenarians was minor analgesics, which were twice as common in centenarians as in octogenarians. In addition, opioids were more frequently used by centenarians than nonagenarians and octogenarians. Hence, centenarians had an overall higher use of analgesics than both nonagenarians and octogenarians. Centenarians also had a high use of hypnotics/sedatives, antidepressants, anxiolytics and laxatives.

The gender differences in drug use in centenarians were generally small and similar to that of octogenarians and nonagenarians. The largest difference was found for antidepressants, which were used by 1 in 5 of the female and 1 in 10 of the male centenarians.

We further explored the association between age and the most commonly used drugs in logistic regression analyses

<table>
<thead>
<tr>
<th>Table 1. Characteristics of the octogenarians, nonagenarians and centenarians stratified by living situation, 2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>Octogenarians (n = 383,876)</td>
</tr>
<tr>
<td>Community dwelling (n = 340,048)</td>
</tr>
<tr>
<td>Mean age (years ± SD)</td>
</tr>
<tr>
<td>Median age (inter-quartile range)</td>
</tr>
<tr>
<td>Sex % (n)</td>
</tr>
<tr>
<td>Men</td>
</tr>
<tr>
<td>Women</td>
</tr>
<tr>
<td>Median number of dispensed drugs (inter-quartile range)</td>
</tr>
</tbody>
</table>
beta-blockers and ACE-inhibitors compared with nonagenarians and octogenarians, but less likely to use antithrombotic agents. However, the association was reversed in the adjusted analysis. Compared with octogenarians and nonagenarians in both the unadjusted and adjusted analyses, centenarians were more likely to use analgesics (i.e., opioids and minor analgesics) than nonagenarians and octogenarians. Further, centenarians were more likely to use high-ceiling diuretics, but less likely to use antithrombotic agents, beta-blockers and ACE-inhibitors compared with nonagenarians and octogenarians.

### Discussion

Our large nationwide study of drug use in old age shows that centenarians use on average a similar number of drugs as octogenarians. Also, institutionalisation increased markedly with age [22]. This raises the question whether centenarians really have less health problems than younger elderly people [5, 6]. Further, centenarians used more analgesics (i.e., opioids and minor analgesics) than nonagenarians and octogenarians. Use of analgesics has been associated with institutionalisation.

### Table 2. Dispensed drug classes in relation to age and living situation, 2008

<table>
<thead>
<tr>
<th>ATC-code</th>
<th>Drug class</th>
<th>Octogenarians (n = 383,878)</th>
<th>Nonagenarians (n = 76,584)</th>
<th>Centenarians (n = 1,672)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Community dwelling (n = 43,830)</td>
<td>Institution dwelling (n = 50,903)</td>
<td>Community dwelling (n = 25,681)</td>
</tr>
<tr>
<td>C03C</td>
<td>High-ceiling diuretics</td>
<td>21.6 (73,379)</td>
<td>38.0 (16,664)</td>
<td>34.7 (17,659)</td>
</tr>
<tr>
<td>N02B</td>
<td>Minor analgesics</td>
<td>16.2 (55,157)</td>
<td>46.9 (20,567)</td>
<td>22.8 (11,603)</td>
</tr>
<tr>
<td>B01A</td>
<td>Antithrombotic agents</td>
<td>46.3 (157,450)</td>
<td>50.8 (22,277)</td>
<td>48.1 (24,503)</td>
</tr>
<tr>
<td>N05C</td>
<td>Hypnotics/sedatives</td>
<td>19.6 (66,640)</td>
<td>33.2 (14,566)</td>
<td>25.8 (13,143)</td>
</tr>
<tr>
<td>A06A</td>
<td>Laxatives</td>
<td>8.6 (29,329)</td>
<td>33.9 (14,863)</td>
<td>13.5 (6,888)</td>
</tr>
<tr>
<td>B03B</td>
<td>Vitamin B12 and folic acid</td>
<td>17.0 (57,697)</td>
<td>30.4 (13,319)</td>
<td>24.0 (12,237)</td>
</tr>
<tr>
<td>N06A</td>
<td>Antidepressants</td>
<td>12.1 (41,054)</td>
<td>46.7 (20,452)</td>
<td>12.4 (6,327)</td>
</tr>
<tr>
<td>C07A</td>
<td>Beta-blockers</td>
<td>38.1 (129,612)</td>
<td>30.3 (13,282)</td>
<td>34.0 (17,326)</td>
</tr>
<tr>
<td>A02B</td>
<td>Drugs for peptic ulcer and gastro-oesophageal reflux</td>
<td>14.4 (48,970)</td>
<td>24.5 (10,721)</td>
<td>15.4 (7,829)</td>
</tr>
</tbody>
</table>

### Table 3. Logistic regression for dispensed drug classes in relation to age, 2008

<table>
<thead>
<tr>
<th>ATC-code</th>
<th>Drug class</th>
<th>Unadjusted analysis, OR (95% CI)</th>
<th>Adjusted analysis*, OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Octogenarians (n = 383,878)</td>
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<tr>
<td></td>
<td></td>
<td>Community dwelling (n = 43,830)</td>
<td>Institution dwelling (n = 50,903)</td>
</tr>
<tr>
<td>C03C</td>
<td>High-ceiling diuretics</td>
<td>Ref 2.01 (1.98–2.05)</td>
<td>2.55 (2.32–2.81)</td>
</tr>
<tr>
<td>N02B</td>
<td>Minor analgesics</td>
<td>Ref 1.87 (1.84–1.90)</td>
<td>2.61 (2.37–2.88)</td>
</tr>
<tr>
<td>B01A</td>
<td>Antithrombotic agents</td>
<td>Ref 1.04 (1.03–1.06)</td>
<td>0.65 (0.59–0.72)</td>
</tr>
<tr>
<td>N05C</td>
<td>Hypnotics/sedatives</td>
<td>Ref 1.50 (1.48–1.53)</td>
<td>1.83 (1.65–2.02)</td>
</tr>
<tr>
<td>A06A</td>
<td>Laxatives</td>
<td>Ref 1.98 (1.94–2.02)</td>
<td>3.21 (2.89–3.57)</td>
</tr>
<tr>
<td>B03B</td>
<td>Vitamin B12 and folic acid</td>
<td>Ref 1.59 (1.56–1.62)</td>
<td>1.68 (1.51–1.87)</td>
</tr>
<tr>
<td>N06A</td>
<td>Antidepressants</td>
<td>Ref 1.37 (1.34–1.39)</td>
<td>1.17 (1.03–1.32)</td>
</tr>
<tr>
<td>C07A</td>
<td>Beta-blockers</td>
<td>Ref 0.77 (0.75–0.78)</td>
<td>0.36 (0.32–0.41)</td>
</tr>
<tr>
<td>A02B</td>
<td>Drugs for peptic ulcer and gastro-oesophageal reflux</td>
<td>Ref 1.19 (1.17–1.21)</td>
<td>1.12 (0.98–1.27)</td>
</tr>
</tbody>
</table>

*Adjusted for sex, living situation and number of other drugs.
[23, 24] and more centenarians than octogenarians and nonagenarians lived in institutions. Therefore, it was surprising to find that centenarians had a higher probability of use of analgesics also after adjustment for living situation. Research about pain in centenarians has given conflicting results; there are findings of both a decreased frequency of pain [25] and comparable levels of pain in centenarians and younger elderly [26]. Our finding of higher use of analgesics in centenarians could reflect an actual increased level of pain in extreme old age or a palliative approach to pain treatment in centenarians. Centenarians’ high use of laxatives might also reflect palliative care and side effects of opioids [27].

In a study of non-institutionalised Finns, centenarians had a lower use of psychotropic drugs than younger elderly people [13]. Conversely, in our study, centenarians used more anxiolytics, hypnotics/sedatives and antidepressants than octogenarians. However, after adjustment for sex, living situation and co-morbidity, centenarians were more likely to use hypnotics/sedatives and anxiolytics, but less likely to use antidepressants than nonagenarians and octogenarians. As with analgesics, our finding of centenarians’ higher use of hypnotics/sedatives and anxiolytics does not support the notion that centenarians are healthier than younger elderly people.

There was a negative association between centenarians and use of antidepressants in the adjusted analysis. However, previous research has revealed that depressive symptoms are more common in centenarians than octogenarians [28]. Depression in extreme old age may be difficult to detect, particularly in patients with dementia. Instead of melancholy, the depression may be expressed as agitation and confusion [29]. This might lead to treatment with anxiolytics and hypnotics/sedatives instead of antidepressants in depressed centenarians.

The cardiovascular drug use also differed between the three age groups. The most commonly used drug class in centenarians was high-ceiling diuretics, which was only half as commonly used by octogenarians. A high use of diuretics has also been reported in Finnish centenarians [14]. Octogenarians and nonagenarians in our study were more likely to use antithrombotic agents, beta-blockers and ACE-inhibitors than centenarians. Hence, centenarians do not seem to be prescribed cardiovascular drug therapy according to guidelines to the same extent as nonagenarians and octogenarians [14, 30]. Use of older types of drugs in centenarians either reflects a cohort or an age effect. That is, drug therapy initiated in younger ages is likely to be continued into old age. Alternatively, physicians might be hesitant to introduce new drugs to very old patients and, consequently, prescriptions for ‘old’ drugs may be routinely renewed (particularly in the institutional setting).

Female centenarians used only slightly more drugs than their male counterparts and the differences in individual drug use were generally small. This might suggest that gender differences in drug use [31] level off in very old age. Also, institutionalisation was a determinant of drug use, although less so for centenarians than for octogenarians and nonagenarians.

The cross-sectional design of our study does not allow us to draw conclusions regarding causality and we cannot differentiate between cohort and age effects. The Swedish Prescribed Drug Register does not include information about over-the-counter drugs, drugs used in hospitals or drugs supplied from drug storerooms, which leads to an underestimation of drug use in the institutional setting. Further, data on dispensed drugs may not adequately reflect what is actually consumed.

Moreover, our method is built on an assumption that all current drugs were dispensed during the observed 3-month period, due to the fact that drugs are prescribed for use during at the most 90 days in Sweden. Therefore, we might have disregarded drugs that were dispensed before the 3-month period and used at a slower rate than intended. At the same time, we might have included drugs that were dispensed during the 3-month period but discontinued prematurely. Also, drug sales have been reported to be lower during the summer [32], which could lead to a general underestimation of drug use in our study. In addition, our method is based on interpretations of the dispensed drugs’ dosages as written by the prescribers, as well as assumptions about DDDs when information about dosage was incomplete or missing [18, 19].

The Swedish Prescribed Drug Register does not include information about the underlying indications or diagnoses for prescription of drugs. Thus, we cannot determine whether certain health conditions were under or over treated. We also lacked data on general health status, although we did control for a proxy for overall co-morbidity (i.e. number of other drugs).

In conclusion, our large nationwide study suggests that the level of drug use in centenarians is comparable with that of octogenarians. Centenarians are more likely to use analgesics, hypnotics/sedatives and anxiolytics than nonagenarians and octogenarians. This may indicate pain and mental health problems in extreme old age. Further research of health status in relation to drug use is needed, to evaluate whether our findings reflect a palliative approach to drug treatment in centenarians.

Also, centenarians do not seem to be prescribed cardiovascular drug therapy according to guidelines to the same extent as nonagenarians and octogenarians. Whether this reflects an age or cohort effect should be investigated in longitudinal studies.

**Key points**

- Although the number of centenarians increases rapidly, little is known about their health and use of medications.
- Centenarians are more likely to use analgesics, hypnotics/sedatives and anxiolytics than nonagenarians and octogenarians.
- Also, different cardiovascular drugs are prescribed to centenarians compared with nonagenarians and octogenarians.
- Thus, centenarians may have a different morbidity profile or they may be treated differently by the health care system.
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Conflicts of interest

None declared.

Ethics committee approval

This study was approved by the ethical board in Stockholm (Dnr 2009/477-31/3) and we only analysed non-identifiable data.

Funding

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References

The relationships between muscle strength, biomechanical functional moments and health-related quality of life in non-elite older adults

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Abstract

Objective: to investigate the association between muscle strength, biomechanical functional moments during everyday tasks and health-related quality of life (HRQoL) in older adults.

Methods: eighty-four healthy adults aged 60–88 years were tested. A torque dynamometer was utilised to measure muscle moments at the knee and hip joints. Functional assessment involved three-dimensional biomechanical analysis of gait, chair rise and sit-down, stair ascent and descent using an 8-camera VICON® system with Kistler force plates. HRQoL was assessed using the Short Form-36 (SF-36) questionnaire.

Results: Spearman’s correlation coefficient showed significant correlation ($P < 0.001$) between isometric strength and functional moments ($r = 0.24–0.67$). Muscle strength was significantly correlated with SF-36 scores, including physical functioning, bodily pain, vitality, social functioning and role emotional scores. Knee flexion moment was correlated with role physical, vitality, social functioning, role emotional, mental health and mental component scores ($r = 0.24–0.40$).

Conclusion: loss of muscle strength is associated with poorer functional ability and both are associated with reduced HRQoL. The reduction in HRQoL is considerable in the physical functioning domain. Cause and effect was not established but studies need to be undertaken to evaluate the benefits of strength training, functional activity training or increased participation in life.

Keywords: muscle strength, grip strength, sarcopaenia, functional ability, moments, ageing, quality of life, physical functioning, SF-36, elderly

Introduction

There is increasing recognition of the impact of loss of muscle strength on health outcomes in older people particularly in terms of increased risk of disability, morbidity, mortality, hospitalisation, falls and significant health-care costs [1–4]. An association between general health (GH) and muscle function in relation to muscle mass [5] and grip strength [6, 7] has been reported in healthy older adults. Research into the relationship between physical performance...