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Drug Utilization and Inappropriate Prescribing in Centenarians

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OBJECTIVES: To use primary care electronic health records (EHRs) to evaluate prescriptions and inappropriate prescribing in men and women at age 100.

DESIGN: Population-based cohort study.

SETTING: Primary care database in the United Kingdom, 1990 to 2013.

PARTICIPANTS: Individuals reaching the age of 100 between 1990 and 2013 (N = 11,084; n = 8,982 women, n = 2,102 men).

MEASUREMENTS: Main drug classes prescribed and potentially inappropriate prescribing according to the 2012 American Geriatrics Society Beers Criteria.

RESULTS: At the age of 100, 73% of individuals (79% of women, 54% of men) had received one or more prescription drugs, with a median of 7 (interquartile range 0–12) prescription items. The most frequently prescribed drug classes were cardiovascular (53%), central nervous system (CNS) (53%), and gastrointestinal (47%). Overall, 32% of participants (28% of men, 32% of women) who received drug prescriptions may have received one or more potentially inappropriate prescriptions, with temazepam and amitriptyline being the most frequent. CNS prescriptions were potentially inappropriate in 23% of individuals, and anticholinergic prescriptions were potentially inappropriate in 18% of individuals.

CONCLUSION: The majority of centenarians are prescribed one or more drug therapies, and the prescription may be inappropriate for up to one-third of these individuals. Research using EHRs offers opportunities to understand prescribing trends and improve pharmacological care of the oldest adults. J Am Geriatr Soc 2016.

Key words: centenarians; epidemiology; inappropriate prescribing; aging; primary care
PIMs within each category was also estimated. The standard criteria were used, rather than the disease-specific criteria, because of the large population-based sample in the study. The three drugs that were most frequently prescribed appropriately were evaluated, and descriptive statistics were used to determine the median number of PIMs in each category. Desiccated thyroid is not listed in the BNF, so it was excluded from the analysis. Glyburide is known as glibenclamide in the United Kingdom. The prescribing of non-steroidal anti-inflammatory drugs (NSAIDs) in this study was considered inappropriate only if, as stated in the 2012 AGS Beers Criteria, they were not taken with a gastroprotective agent. All topical non-cyclooxygenase-selective NSAIDs were not considered as inappropriate and only oral formulations were included, as stated by the 2012 AGS Beers Criteria.

RESULTS

A cohort of 11,047 centenarians (8,982 women, 2,102 men), who reached the age of 100 between 1990 and 2013, was selected for analysis. Eighty-four percent were born between 1900 and 1913 and the remaining 16% between 1890 and 1899. The median annual number of prescriptions was 7 (interquartile range 0–12) during the 100th year.

Table 1 shows the most frequently prescribed drugs at the age of 100. Drug utilization for each drug class was higher in women than in men, except for urinary tract drugs.

Table 1. Frequency of Different Categories of Prescriptions According to Sex

| Drug Class from British National Formulary | Female, n = 8,982 | Male, n = 2,102 | All, N = 11,084 |
|------------------------------------------|------------------|----------------|---------------|
| Any                                      | 6,904 (79)       | 1,136 (54)     | 8,040 (73)    |
| Cardiovascular                           | 5,044 (56)       | 835 (39)       | 5,879 (53)    |
| Central nervous system<sup>a</sup>       | 5,182 (58)       | 741 (35)       | 5,923 (53)    |
| Gastrointestinal                         | 4,488 (50)       | 752 (36)       | 5,240 (47)    |
| Skin                                     | 3,524 (39)       | 537 (26)       | 4,061 (37)    |
| Nutrition and blood                      | 3,485 (39)       | 479 (23)       | 3,964 (36)    |
| Antimicrobial                            | 4,028 (45)       | 631 (30)       | 4,659 (42)    |
| Eye                                      | 2,038 (23)       | 316 (15)       | 2,354 (21)    |
| Musculoskeletal and joint diseases       | 1,963 (22)       | 307 (15)       | 2,270 (20)    |
| Endocrine                                | 1,818 (20)       | 283 (13)       | 2,101 (19)    |
| Respiratory                              | 1,545 (17)       | 277 (13)       | 1,822 (16)    |
| Anesthesia                               | 1,131 (13)       | 198 (9)        | 1,329 (12)    |
| Ear, nose, oropharynx                    | 828 (9)          | 171 (8)        | 999 (9)       |
| Immunologial products and vaccines       | 786 (9)          | 119 (6)        | 905 (8)       |
| Gynecological and urinary tract          | 692 (8)          | 206 (10)       | 898 (8)       |
| Neoplasms and immunosuppression          | 497 (6)          | 92 (4)         | 589 (5)       |

<sup>a</sup>Frequency of individuals with at least one prescription during the year they turned 100.

<sup>b</sup>Hypnotics, anxiolytics, antidepressants, analgesics, drugs for nausea and vertigo, antiepileptics, drugs for parkinsonism and dementia.
The frequency of PIP according to the 2012 AGS Beers Criteria is presented in Table 2. Overall, 32% of centenarians were prescribed a PIM, and the three most frequently prescribed PIMs were temazepam, amitriptyline, and nitrofurantoin. The drug class with the highest proportion of PIP was CNS medications (23%). Approximately one-fifth of centenarians (19% women, 13% men) received anticholinergic drugs, with PIMs including chlorphenamine, hydroxyzine, and promethazine hydrochloride. Despite the high levels of prescribing for gastrointestinal, cardiovascular, and analgesic drugs, low levels of inappropriate prescribing (5%) were observed within these classes.

**DISCUSSION**

To the knowledge of the authors, this is the first population-based study describing medication use and PIP in centenarians. Only a minority of centenarians did not receive prescription medicines, with a higher proportion of men not receiving any prescriptions, consistent with their superior health status at age 100. Almost 80% of women and 54% of men were prescribed at least one drug during their 100th year. Sex differences in overall prescribing between centenarians have not been reported previously. This disparity could be because of sex differences in health-seeking behavior, for example, not seeking a physician’s advice, or nonadherence, as well as resulting from differences in health status. Up to one-third of centenarians were prescribed a PIM. The highest frequencies of PIP were attributed to the use of benzodiazepines (temazepam, diazepam), amitriptyline, and nitrofurantoin. The 2012 AGS Beers Criteria recommendation to avoid all of these drugs is “strong,” and the reported quality of evidence is “high” for avoiding temazepam, diazepam, and amitriptyline and “moderate” for avoiding nitrofurantoin. The 2012 AGS Beers Criteria recommend avoiding nitrofurantoin in individuals with creatinine clearance less than 60 mL/min because of concerns about lack of efficacy from inadequate drug concentrations in the urine. In view of the advanced age of the cohort, it is likely that most will have poor renal function and should therefore be using safer alternatives such as ciprofloxacin or trimethoprim.

**Comparison with Existing Literature**

Existing studies on drug utilization in elderly adults have often focused on younger cohorts of old people or do not include centenarians. There is scarce evidence about PIP in extreme old age. These studies focusing on younger elderly adults tend to rely on self-reported questionnaires and interviews, resulting in a high risk of responder bias.

There have been no previous studies reporting PIP in a large group of centenarians. Reports of prevalence of PIP in individuals aged 65 and older are inconsistent, and few studies have used the updated 2012 criteria. One study using the 2012 criteria reported a higher prevalence of PIP (44%) in Spanish individuals aged 65 and older than the present findings (32%) in centenarians. The most frequently prescribed PIMs were benzodiazepines, similar to the present data. Another study in New Zealand also reported a higher PIM prevalence (42.7%) for community-dwelling individuals aged 75 and older than for those aged 100 and older in CPRD, whereas another study reported a prevalence of 17%. All three studies used self-reported data. Several studies reported pain medications as the most commonly prescribed PIMs, including two studies using the Screening Tool of Older People’s potentially inappropriate Prescriptions/Screening Tool to Alert doctors to the Right Treatment (STOPP/START) criteria. This is inconsistent with the present findings in centenarians, reporting CNS medications and anticholinergics as the most commonly prescribed PIMs. It is not stated in all these previous studies whether concurrent use of gastroprotective agents was considered alongside NSAIDs.

**Strengths and Limitations**

This study had the strengths of a large sample drawn from a representative population of U.K. general practices. In the United Kingdom, approximately 98% of individuals are registered with a family practice, ensuring that the present data are complete and nationally representative. Individuals aged 75 and older have an annual review of medicines, and those with four or more medicines are reviewed every 6 months, although this review was not introduced until 2002. Using primary care EHRs allowed for the classification of prescribing according to drug category and of specific PIMs, but data were not available for several variables of interest, including whether an individual lived alone or whether they lived in an urban or rural location. EHRs circumvent the problem of recall bias, a limitation of many drug use studies relying on self-reported questionnaires or interviews to collect data on prescrip-
| Drug Category          | Total Drug Class, n\(^a\) | Female, n = 8,982 | Male, n = 2,102 | All, N = 11,084 |
|------------------------|-----------------------------|-------------------|-----------------|-----------------|
|                        | Number of PIMs, Median (IQR) | Top 3 PIMs        | Number of PIMs, Median (IQR) | Top 3 PIMs        | Number of PIMs, Median (IQR) | Top 3 PIMs        |
| Any                    | 6,799                       | 2,208 (32)        | 5 (2–12)        | 1,108           | 309 (28)        | 4 (1–10)        | 7,907           | 2,517 (32)        | 5 (2–12)        |
| Central nervous system | 5,182                       | 1,240 (24)        | 7 (2–13)        | 741             | 147 (20)        | 5 (2–12)        | 5,923           | 1,387 (23)        | 6 (2–12)        |
| Anticholinergic        | 1,279                       | 237 (19)          | 2 (1–8)         | 219             | 28 (13)         | 2 (1–6)         | 1,498           | 265 (18)          | 2 (1–7)         |
| Anti-infective         | 4,027                       | 353 (9)           | 1 (1–2)         | 631             | 38 (6)          | 1 (1–2)         | 4,668           | 391 (8)           | 1 (1–2)         |
| Analgesic              | 5,348                       | 258 (5)           | 2.5 (1–7)       | 844             | 31 (4)          | 1 (1–2)         | 6,192           | 289 (5)           | 2 (1–6)         |
| Gastrointestinal       | 4,653                       | 238 (5)           | 1 (1–4)         | 773             | 31 (4)          | 1 (1–2)         | 5,426           | 269 (5)           | 1 (1–3)         |
| Cardiovascular         | 5,044                       | 207 (4)           | 7 (3–13)        | 835             | 50 (6)          | 6 (3–11)        | 5,879           | 257 (4)           | 7 (3–13)        |
| Antithrombotic         | 2,578                       | 87 (3)            | 6 (2–12)        | 460             | 26 (6)          | 6 (2–12)        | 3,038           | 113 (4)           | 6 (2–12)        |
| Endocrine              | 1,888                       | 15 (1)            | 11 (3–13)       | 311             | 1 (0.3)         | 6 (6–6)         | 2,199           | 16 (0.1)          | 9 (4–13)        |

\(^a\)Number of individuals from total sample with at least one prescription during the year of turning 100 years old in each overall Beers category.

\(^b\)PIMs = potentially inappropriate medications within each Beers category as defined by the 2012 AGS Beers Criteria (row percentages).
tions. There is a possibility that some prescriptions will not be filled or consumed, and the data may not capture any over-the-counter or secondary care hospital prescriptions, so the present findings may underestimate drug usage of centenarians. Another limitation is that the sample was exposed to a nonuniform drug formulary because the study considers data over a 23-year span. Medical practice in primary care has evolved over time, and as a result, certain drugs used in 1990 may now be considered inappropriate. Several new drugs have also been introduced that could not be prescribed in 1990.

There are limitations of the 2012 AGS Beers Criteria, given their universal application without careful consideration of an individual’s response to each drug. There may also be some drugs used in the United Kingdom that were not captured. In 2003, the STOPP/START criteria were developed to identify potential errors in prescribing and prescribing omission in older people according to physiological system. These criteria were created as a Europe-focused tool but are not as widely used as the 2012 AGS Beers Criteria to evaluate the epidemiology of PIP because of their specificity. Although a more-individualized tool may be favored in clinical practice, this approach is less feasible for epidemiological investigation of population-based samples. The 2012 AGS Beers Criteria were specifically designed to use pharmacy records with minimal additional clinical information so that they could be applied to chart reviews or computerized data sets.

According to the 2012 AGS Beers Criteria, the most commonly prescribed PIMs in the present cohort were benzodiazepines, tertiary tricyclic antidepressants, nitrofurantoin, and ibuprofen. The frequencies of PIP found in this study should be interpreted cautiously because each person’s risk:benefit ratio for a drug will depend on his or her physiological and clinical status. Only an individual evaluation of each person will confirm the validity of these interpretations. Nevertheless, population-based studies provide useful epidemiological data on relative frequencies of PIP in large cohorts and help identify the inappropriate medications that are most frequently prescribed. This study also identifies specific drugs that may be given more attention in further research on the determinants of PIP in elderly adults.

Conclusion and Implications for Clinical Practice

Polypharmacy and multimorbidity in elderly adults present health professionals with a significant clinical responsibility. The limited empirically based evidence to guide drug prescription in very old adults means that physicians must base their prescribing decisions on clinical knowledge and prior experience with similar conditions, likely from younger cases. There is an urgent need for studies to explore the efficacy, safety, and harms associated with drug prescribing for different chronic conditions in very old adults. There is also the need to model the adverse clinical and economic consequences of inappropriate therapeatic decision-making in this group.

This is the first study to use primary care EHR data to describe prescribing trends in UK centenarians, as well as the extent of PIP according to drug class. It provides proof of concept for using a large EHR database to evaluate appropriateness of prescribing and a basis for reevaluating indicators of appropriate prescribing as applied to this age group. This also offers valuable data for the modeling of future healthcare needs and costs of the oldest adults in the United Kingdom.

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Conflict of Interest: The study is based in part on data from the CPRD obtained under license from the U.K. Medicines and Healthcare products Regulatory Agency, but the interpretation and conclusions contained in this report are those of the authors alone. There are no conflicts of interest involved. The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this paper.

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