CLINICAL RESEARCH STUDY

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Choosing Wisely? Measuring the Burden of Medications in Older Adults near the End of Life: Nationwide, Longitudinal Cohort Study

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ABSTRACT

BACKGROUND: The burden of medications near the end of life has recently come under scrutiny, because several studies suggested that people with life-limiting illness receive potentially futile treatments.

METHODS: We identified 511,843 older adults (>65 years) who died in Sweden between 2007 and 2013 and reconstructed their drug prescription history for each of the last 12 months of life through the Swedish Prescribed Drug Register. Decedents' characteristics at time of death were assessed through record linkage with the National Patient Register, the Social Services Register, and the Swedish Education Register.

RESULTS: Over the course of the final year before death, the proportion of individuals exposed to ≥10 different drugs rose from 30.3% to 47.2% (P <.001 for trend). Although older adults who died from cancer had the largest increase in the number of drugs (mean difference, 3.37; 95% confidence interval, 3.35 to 3.40), living in an institution was independently associated with a slower escalation ($\beta = -0.90$, 95% confidence interval, −0.92 to −0.87). During the final month before death, analgesics (60.8%), antithrom-botic agents (53.8%), diuretics (53.1%), psycholeptics (51.2%), and β-blocking agents (41.1%) were the 5 most commonly used drug classes. Angiotensin-converting enzyme inhibitors and statins were used by, respectively, 21.4% and 15.8% of all individuals during their final month of life.

CONCLUSION: Polypharmacy increases throughout the last year of life of older adults, fueled not only by symptomatic medications but also by long-term preventive treatments of questionable benefit. Clinical guidelines are needed to support physicians in their decision to continue or discontinue medications near the end of life.

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Ethical Approval: This study was approved by the Ethical Review Board in Stockholm, Sweden.

Availability of Data and Materials: Clinical data and individual data from the Swedish Prescribed Drugs Register data cannot be made publicly available. Interested researchers can access the aggregated data from the Swedish Prescribed Drugs Register (http://www.socialstyrelsen.se/statistik/statistikdatabas/lakemedel).

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Under the combined effect of increased longevity, chronic multimorbidity, and single-disease clinical guidelines, the concomitant use of multiple medications has become commonplace among older adults.[1] Polypharmacy increases inappropriate drug use and drug−drug interactions and exposes older adults to serious adverse effects.[2] Yet, it is estimated that 25% to 40% of adults aged 65 years or older are prescribed at least 5 medications.[3]

When considering older people near the end of life, poly-pharmacy poses 2 problems. First, as death approaches, age-related physiologic changes are amplified by the changing metabolism, the decline of renal and hepatic functions, and the loss of body mass. As a result, pharmacokinetics and pharmacodynamics are altered, making older adults with life-limiting illness particularly vulnerable to the harmful side effects of medications.[4] Second, the accumulation of prescriptions in the context of limited life expectancy raises questions about the intended or expected benefit of the treatments.[5]

CLINICAL SIGNIFICANCE

- The burden of medications increases near the end of life (47.2% of older adults receive ≥10 prescription drugs during their last month of life).
- Polypharmacy is fueled not only by symptomatic medications but also by long-term preventive treatments of questionable benefit.
- Guidelines are needed to support physicians in their decision to continue or discontinue drug treatments near the end of life.

The burden of medications near the end of life has recently come under scrutiny, because several studies have shown that people with specific life-limiting diseases are prescribed medications whose benefit is unlikely to be achieved within their remaining lifespan.[6] However, these studies have all been conducted in selected samples of individuals who shared a common disease[7-10] or care setting[11-14] or were recruited for a clinical trial.[15] Future research and clinical guidelines need to be informed by findings that are generalizable beyond a specific illness or care setting.

This study aimed to measure the change in the prevalence of polypharmacy and to identify the most commonly used medications over the course of the last year of life of older people, using data with national coverage in Sweden.

METHODS

Study Design and Population

We conducted a nationwide, follow-back cohort study of all older adults who died at age >65 years in Sweden between January 1, 2007 and December 31, 2013. Individuals were excluded from the study population if they had no reported cause of death or had no prescription data available during the final 3 months before the date of death (Supplementary Figure 1, available online). Death certificate data were obtained from the Swedish National Board of Health and Welfare and were linked at the individual level to several other registries with national coverage: the Swedish Prescribed Drug Register, Social Services Register, National Patient Register, and Swedish Education Register. Data were anonymized, and the Regional Ethical Review Board in Stockholm approved the study (no. 2013/1941-31/3 and 2015/1319-32).

Assessment of Polypharmacy and Drug Exposure

Polypharmacy was considered as the primary outcome. Although there is no consensual definition, studies conducted in the general geriatric population typically use a threshold of ≥4 or ≥5 medications to characterize polypharmacy and ≥9 or ≥10 to describe "excessive polypharmacy."[16-18] In light of the considerable burden of chronic diseases and symptoms near the end of life,[19] we opted for the latter, more conservative cut-off. Hence polypharmacy was hereafter defined as the monthly exposure to 10 or more prescription drugs, that is, distinct substances according to the fifth level of the Anatomical Therapeutic Chemical (ATC) classification system.

Prescription drug data were derived from the Swedish Prescribed Drug Register to evaluate the total number of medications during each of the final 12 months before death. In Sweden, drug prescriptions cover a maximum period of 90 days. Drug exposure was estimated according to 1) the date of dispensing, 2) the total amount dispensed to the patient, and 3) the prescribed daily dose, as described in Supplementary Figure 2 (available online).[20,21] In addition, we calculated the prevalence of the 20 most common individual drug classes for the 12th, 6th, and final months before death. As recommended by the World Health Organization, drugs were classified by ATC code.

Descriptive Variables

Sex and age at time of death were both extracted from death certificates. International Classification of Diseases, 10th revision diagnosis codes for all contributing causes of death were categorized into 4 distinct "illness trajectories" indicative of the potential timeframe of care needs near the end of life: cancer, organ failure, prolonged dwindling, and sudden death.[22,23] Individuals were assigned a single illness trajectory using a modified version of the protocol developed by Lunney et al[24] (Supplementary Table 1, available online). When multiple causes of death indicated more than 1 illness trajectory, we applied a predefined hierarchy (ie, from cancer to prolonged dwindling to organ failure to sudden death).[25] In addition, we used a multimorbidity assessment tool recently validated in the general elderly