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Update on Medication Use Quality and Safety in Older Adults, 2017

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Abstract

Improving the quality of medication use and medication safety in older adults is an important public health priority and is of paramount importance for clinicians who care for them. We selected four important articles from 2017 that address these issues to annotate and critique, and we discuss the broader implications for optimizing medication use. A longer list of articles is given in an online appendix. The first study provides national data on the prevalence of central nervous system–active medication polypharmacy in older adults and how this has changed over a 9-year period (2004–2013). The second study characterizes prevalence of and factors associated with nonadherence to antiepileptic drugs in 36,912 older adults with epilepsy, with an emphasis on

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article.

Supplementary Appendix S1. Important articles from 2017 that addressed quality and safety of medication use in older adults.

Supplementary Appendix S2. List of journals manually searched.

minorities. The third study describes the extent of antibiotic use in residents of 381 long-term care facilities (LTCF) in British Columbia, Canada, from 2007 to 2014. Finally, we discuss a meta-analysis of 42 studies that evaluated the prevalence of hospital admissions caused by adverse drug reactions in older adults. This article is intended to provide a narrative review of important publications on medication use quality and safety for clinicians and researchers committed to optimizing medication use in older adults.

Keywords

drug-related problems; polypharmacy; inappropriate prescribing; adverse drug events

Optimal medication use is a priority for healthcare providers caring for older adults. Clinicians face the ongoing challenge of prescribing evidence-based therapy while trying to avoid unnecessary polypharmacy—often resulting in concomitant overprescribing and underprescribing in the same person.[1] Although pharmacotherapy can improve quality of life and reduce mortality, suboptimal pharmacotherapy can increase the risks of adverse drug events (ADEs).

A monumental challenge to optimizing medication use is the absence of information regarding efficacy and safety of medications in older adults. Older adults are infrequently included in randomized controlled Phase III efficacy trials of new drugs even if they are targeted for medical conditions confined to or highly prevalent in this age group.[2] Furthermore, the number of people enrolled in clinical trials is insufficient to detect rare ADEs, including geriatric syndromes.[2] In the absence of such information, clinicians are left to extrapolate available medication information from observational studies and other age groups and to use guiding geriatric medication principles to achieve medication effectiveness while attempting to avoid medication risks.[3–5]

Identifying articles addressing quality of medication use and medication-related problems is also challenging because of lack of specific search terms in computerized databases. Therefore, the objective of this special report was to conduct an extensive search of the literature to identify important articles that addressed these problems during 2017 (Supplementary Appendix S1) that we hope will be of interest to readers. We selected 4 of these articles to annotate and critique and to discuss the broader implications for optimizing medication use.

METHODS

A search using OVID was conducted, restricted to articles published in 2017, English language, humans, and older adults (65 and over) using a combination of the following terms: adverse drug events, adverse drug reactions, adverse drug withdrawal events, deprescribing, drug-related problems, inappropriate prescribing, medication adherence, medication administration, medication dispensing, medication errors, medication misadventures, medication monitoring, medication-related problems, polypharmacy, suboptimal prescribing, therapeutic failure, underutilization, and unnecessary drugs. We included studies that used rigorous observational/experimental designs and reliable/valid

measures. A similar search was conducted using Google Scholar. In addition, we performed a manual search for relevant articles from select high impact journals (Supplementary Appendix S2). Finally, we identified additional articles from our files. We excluded studies published by the authors and those appearing in journals that regularly publish articles related to these topics and thus are more easily identified by readers (i.e., Consultant Pharmacist, Drugs and Aging and the Journal of the American Geriatrics Society).

RESULTS

One hundred fourteen articles were identified. After reviewing the abstracts and removing duplicates, we selected 67 articles for inclusion in this review (Supplementary Appendix S1). Two authors (SLG, JTH) independently reviewed the full text of these 67 articles and chose 4 that were thought to be particularly unique and important to describe further and critique below.

Central Nervous System–Active Polypharmacy in Older Adults

One article examined the prevalence of U.S. outpatient physician visits in which 3 or more central nervous system (CNS)-active medications were prescribed from 2004 through 2013.[6] The data source was the National Ambulatory Medical Care Survey, and the sample was restricted to individuals aged 65 and older (N = 97,910). The authors recorded up to 3 diagnoses and 8 medications for each person. The primary outcome measure was CNS polypharmacy defined according to the 2015 American Geriatrics Society Beers drug interaction criteria that 3 or more of the following medications were initiated or continued: antidepressants (e.g., tricyclic antidepressants, selective serotonin reuptake inhibitors), antipsychotics, benzodiazepine receptor agonists (including “Z-drug” hypnotics), and opioid receptor agonists.[3] Trends over time were examined using logistic regression. In addition, for the last 3 years of data (2011–2013), visit characteristics were compared according to CNS polypharmacy status using difference-in-proportion tests.

The authors found that encounters for CNS polypharmacy increased over the 9-year period (adjusted odds ratio=3.12; 95% confidence interval (CI)=2.28–4.28). For example, CNS polypharmacy occurred at 0.6% of visits during 2004 to 2006 and 1.4% visits during 2011 to 2013. Of the 13 independent variables examined, the largest increases in CNS polypharmacy were in individuals living in rural areas and those with pain. An increase was not observed in those with insomnia or anxiety. In the analyses restricted to the last 3 years of data, fewer than 7% of those with CNS polypharmacy visits received psychotherapy or stress management or health education. In a sensitivity analysis in which opioids were not included in the CNS poly-pharmacy measure, anxiety (10.8% vs 30.6%, $p < .001$) and depression (0.6% vs 9.6%, $p < .001$) were less common than with the full measure. In the Discussion section, the authors highlight that overprescribing of opioids in the United States might help explain the finding that individuals with a pain diagnosis had a significant increase in CNS polypharmacy over the study period. They also comment that limited access to mental health or pain specialists may help explain the increase in polypharmacy in rural areas.

The authors are to be commended for conducting this national study with a large sample size, which improves generalizability. Unfortunately, other than the use of opioids, the

contribution of individual therapeutic classes to CNS polypharmacy cannot be determined. Readers interested in learning more about this are referred to 2 additional publications by the same group of authors using the same data sources.[7,8] Because of the nature of the data, the unit of analysis is not the percentage of the U.S. population of older adults with evidence of CNS polypharmacy but the percentage of outpatient visits. A population-based cohort study reported that the 4.3% were taking 2 or more CNS active medications in 2002–03.[9] One concern with the study discussed here was its choice of multivariable logistic regression analysis that controlled only for age, sex, race, and ethnicity as opposed to using generalized estimating equation models that examine all demographic, clinical and visit characteristics. Because correlation of variables over time was not accounted for and only a few select control variables were included, the prevalence rates may not be accurate. Moreover, the rate of CNS polypharmacy may be an underestimate because only the first 8 medications were recorded, and other medications affecting the CNS were not included (e.g., mood stabilizers, other antidepressants). Nonetheless, the concern that this article raises is important because CNS polypharmacy increases the risk of falls and cognitive and functional decline.[10,11] Moreover, opioids in combination with benzodiazepines and perhaps certain antiepileptic drugs (AEDs) (e.g., gabapentin, pregabalin) increase the risk of respiratory depression and mortality.[12] Further evidence of its importance is that the Pharmacy Quality Alliance has developed a performance measure to address CNS polypharmacy (https://pqaalliance.org/measures/default.asp).

Adherence to AEDs in Diverse Older Adults

A retrospective analysis of Medicare claims was conducted to examine prevalence of and factors associated with non-adherence to AEDs in older adults with epilepsy, with an emphasis on minorities.[13] The sample consisted of a 5% random sample of beneficiaries augmented by minority representation for claims during 2008 to 2010; 36,912 epilepsy cases with at least 1 year of follow-up were identified and served as the primary analysis. Medication adherence was measured using the proportion of days covered method, with nonadherence defined as a proportion of days covered of less than 0.80. Any AED prescription filled was considered for defining medication adherence.

The sampling scheme resulted in a diverse racial and ethnic distribution of cases: 9.2% white, 62.5% black, 11.3% Hispanic, 5.0% Asian, and 2.0% American Indian or Alaska Native. Most individuals with epilepsy were female (61.6%), lived in the south (50.3%), and were eligible for the Part D Low Income Subsidy (82.0%). The overall prevalence of AED nonadherence was 31.8%, which varied according to race and ethnicity, with the highest nonadherence for blacks (34.3%) and the lowest for whites (24.1%). In adjusted logistic regression models, all minority groups were more likely to be nonadherent to AEDs than whites. Other factors associated with AED nonadherence were aged 85 and older (vs 65–74), 4 or more comorbid conditions (vs 0), taking an enzyme-inducing AED (older agents such as carbamazepine, phenytoin vs non-enzyme-inducing AEDs), being in a deductible phase of their drug benefit (vs those in cost-sharing phases), and being from a high-poverty ZIP code. The authors comment that it is important to be aware of the benefit phase a person is in immediately before filling an AED prescription because this may identify a high-risk period for nonadherence.

These results are largely consistent with an extensive body of literature on medication nonadherence in general and specifically to AEDs, showing that medication nonadherence is common in older adults and disproportionately affects minorities.[14] These differences existed even after adjusting for some socioeconomic factors, although claims data do not completely capture potential confounding by socioeconomic factors, such as access to care and beliefs about medications. Despite that, a major strength of this study was augmentation of the sample with minority beneficiaries, leading to a diverse sample of older adults with epilepsy, a segment of the population that has been understudied.

Adherence to AED regimens is critical for seizure control, and efforts are needed to address modifiable risk factors for nonadherence, in particular those that might vary according to minority status. Consistent with this study's findings, socioeconomic factors and medication cost have consistently been shown to affect medication adherence in older adults across therapeutic classes.[15] One of the biggest barriers to addressing cost-related challenges affecting medication use is the complexity of prescription coverage in the United States, which often leads to a lack of transparency and confusion for older adults. Efforts are needed to increase transparency about out-of-pocket drug costs at the point of prescribing to reduce downstream cost-related non-adherence. A limitation of this study, as the authors highlight, is that medication adherence may be overestimated because claims measure only filled prescriptions and may not reflect actual medication-taking behavior. Moreover, medication adherence is a dynamic health behavior, changing over time, so an average measure such as proportion of days covered may miss some of the nuanced underlying behavior, and using other techniques, such as group-based trajectory modeling, may make it more possible to describe longitudinal AED adherence patterns.[16] Nonetheless, this article reminds us that belonging to a minority group and the presence of certain socioeconomic factors, even in the era of Part D coverage, are barriers to optimal AED adherence in older adults. Prescribers should be aware of the most common modifiable barriers, such as cost, to address them during clinical encounters.

Use of Antibiotics in Long-Term Care Facilities

To describe the extent of antibiotic use of long-term care facility (LTCF) residents in British Columbia, Canada from 2007 to 2014, antibiotic prescription data were used from the PharmaNet centralized data system that links all community pharmacies in British Columbia, including data from the pharmaceutical coverage plan for LTCF residents and linked data from the physician billing plan to obtain indications for the antibiotics.[17] The long-term care population denominator was determined from the British Columbia Ministry of Health Home and Community Care database that records individuals staying at one of British Columbia's LTCFs. Antibiotics were classified based on the World Health Organization (WHO) Anatomical Therapeutic Chemical classification system. Defined daily dose (DDD) was used to calculate rates of use for every 1,000 long-term care residents. The DDD is a measure of drug consumption that the WHO defines based on the usual dose of medications and makes it possible to compare drug use of different drugs. Trends for antibiotic prescribing were examined for 3 indications: urinary tract infections (UTIs), respiratory tract infections (RTIs), and skin and soft tissue infections (SSTIs). The study

database yielded 381 LTCFs with an annual average of nearly 24,694 residents and 419,036 antibiotic prescriptions.

More than half of all residents in LTCFs (60.5%) were prescribed antibiotics. The results showed that antibiotic use did not change significantly over the study period and ranged from 39.2 DDD per 1,000 residents (2007) to 35.2 DDD per 1,000 residents (2014). Of the 3 indications examined, UTIs were the most common indication (6.6 DDD per 1,000 residents), with the most commonly prescribed antibiotics being nitrofurantoin, ciprofloxacin, and trimethoprim/sulfamethoxazole. The next most frequent indication was RTIs (5.3 DDD per 1,000 residents), with moxifloxacin being the most commonly prescribed antibiotic. Rates of treatment for upper RTIs declined significantly over the study period but still remained higher than lower RTIs. Duration of antibiotic therapy in LTCF residents in 2014 was 7.3 days per prescription, which was a significant decrease from 9.3 days in 2007.

This study was notable in that it examined trends in recent antibiotic prescriptions, including dose, over a 7-year period in the full population of LTCF residents in British Columbia. The study confirmed that antibiotic use is highly prevalent in LTCFs. Although antibiotics used for appropriate indications for appropriate duration of therapy are beneficial in treating infections in LTCF residents, antibiotic use is also associated with ADEs, the emergence of multidrug-resistant organisms and the development of *Clostridium difficile* infection. An important concern that this study does not address is the appropriateness of antibiotic use in LTCFs. The rate of antibiotic treatment for upper RTIs, which are usually viral, was higher than for lower RTIs, and other investigators have reported inappropriate use of antibiotics for asymptomatic bacteriuria in LTCFs.[18,19] Generalizability to other countries like the United States is unknown. Nonetheless, these findings highlight the critical importance of vigorous antibiotic steward-ship programs and infection control practices in LTCFs to reduce inappropriate use of antibiotics and development of multi-drug-resistant organisms. The investigators reported a significant decrease in duration of antibiotic therapy in LTCFs over the study period. British Columbia initiated a provincewide antimicrobial stewardship program directed toward providers and the public in 2005 that resulted in reduction in duration of antibiotic therapy between 2007 and 2014 across the province that probably contributed to similar reductions in LTCFs. Important elements of antibiotic stewardship include interprofessional teamwork, depre-scribing, shorter duration of therapy, and narrowing the spectrum of antibiotics.[20] These sustained actions will help optimize antibiotic use in LTCFs.

Hospital Admissions Due to Adverse Drug Reactions

Oscanoa and colleagues performed a systematic review and meta-analysis of studies that evaluated the prevalence of adverse drug reaction (ADR)-related hospital admissions in individuals aged 60 and older.[21] The search spanned from 1988 to 2015, and from 2,060 identified articles, 42 studies met the inclusion criteria and were included in the meta-analysis. Two reviewers independently extracted relevant information using a common data extraction template. The studies were conducted in 21 countries, with the majority being in

Europe (n = 23, 55%) and North America (n = 8, 19%). Most studies assessed causality of the ADR (83%), with a variety of algorithms used.

The mean prevalence of ADR-related hospital admissions was 8.7% (95% CI=7.6–9.8%). Only 14 studies provided information about the implicated medications. From these, the authors noted that NSAIDs were among the most common classes related to hospital admissions, which ranged from 2.5% to 33.3% in the studies. Other medications implicated in ADRs included beta-blockers (1.8–66.7%), antibiotics (1.1–22.2%), oral anticoagulants (3.3 to 55.6%), digoxin (1.6–18.8%), angiotensin-converting enzyme inhibitors (5.5–23.4%), oral antidiabetics (4.5–22.2%), and opioids (1.5–18.8%). Risk factors for ADR-related hospitalizations included number of medications (22 of 22 studies), number of comorbidities (4 of 13), female sex (6 of 21), age (6 of 22), and inappropriate medications (4 of 9). Considerable heterogeneity was found when examining subgroups such as sample size and location. For example, the greatest prevalences of ADR-related hospitalization were in Africa (20.1%) and Latin America (14.7%) and the lowest in Asia (4.3%), the United States (4.2%), and Canada (4.4%).

Approximately 1 in 10 hospitalizations in older adults was related to ADRs, which confirms findings from prior systematic reviews.[22,23] This is the first meta-analysis to our knowledge that has attempted to delineate the most common medication classes responsible for ADR-related hospitalizations, although the authors provided only the range of class-specific ADRs across studies and not an average estimate, which would have provided more useful information for comparisons. Furthermore, the studies had wide variability and overlapping ranges among the medication classes. Another notable finding is that use of inappropriate medications was not a consistent risk factor for ADR-related hospitalizations. This finding is consistent with prior work in which inappropriate medications were found to be implicated in only 1.8% of emergency department visits for ADEs.[24] More than half of the studies were published before 2010. Thus, adding a sensitivity analysis that stratified according to publication year (e.g., use of more current datasets) would have enhanced this study because it might have yielded estimates more reflective of current practice given the increased in efforts focused on ADR prevention in older adults. Furthermore, given the temporal changes in medication use, focusing on contemporary studies is needed to understand the most common medications implicated in ADR-related hospitalizations. Nonetheless, these findings remind us that ADRs continue to remain a significant healthcare problem for older adults. Efforts should focus on prevention of ADRs, especially for medications that have a narrow therapeutic index or require more frequent monitoring (anticoagulants, oral diabetic agents, opioids).[24] Number of medications is a consistent risk factor for ADRs, so periodic medication review and deprescribing of unnecessary medications is of critical importance. Interventions to optimize medication use in older adults are effective in reducing ADRs.[25]

DISCUSSION

We identified numerous studies addressing quality of medication use and medication-related problems in older adults published during 2017. The selected literature has direct application to support change in practice targeting medication safety. The first study highlighted the increase in CNS polypharmacy in older adults. Another study demonstrated that adherence

to AEDs was lower in minorities and individuals of lower socioeconomic status and the need for greater understanding about disparities that contribute to these differences in nonadherence. The third study demonstrated the extent of antibiotic usage in LTCFs in British Columbia. The last study demonstrated that ADRs are a common cause of hospitalizations in older adults. Together, these studies, along with the supplemental bibliographic material (Supplementary Appendix S1) highlights the continued challenge of optimizing medication use and reducing medication risk in older adults. Greater awareness of these medication safety findings is needed to initiate individual-and system-level strategies to address unnecessary, ineffective, and harmful prescribing. Doing so will require a person-centered team approach leveraging existing systems to improve overall safety in the medication use process of initiating, monitoring, and discontinuing medications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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