Adverse drug reactions in the Veterans Affairs healthcare system: Frequency, severity, and causative medications analyzed by patient age

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Purpose. Adverse drug events (ADEs) in the U.S. Department of Veterans Affairs (VA) were evaluated, and differences in age group report rates and reported medications in different age groups were assessed.

Methods. We utilized the VA Adverse Drug Event Reporting System (ADERS) to assess 10-year age groups regarding ADE reporting rates, event severity, and associated reported medications. Data were derived from 484,351 ADE reports from 395,703 patients included in VA ADERS from 2009 through 2016.

Results. Reported rates of ADEs per 10,000 unique users demonstrated a nonlinear relationship with age, peaking in the group aged 60–69 years (148.6 reports/10,000 unique users) and declining thereafter. However, the percentage of adverse events reported as severe consistently rose with age group (3% in patients age 20–29 years versus 6% in patients older than 90 years). The types of medications reported as causative agents shifted over time from predominantly mental health and pain medications in younger veterans (e.g., age 20–29 years) to medications for chronic diseases in older cohorts (e.g., age 60–69 years).

Conclusion. An analysis of VA ADE reports revealed a nonlinear relationship between age and events, with events peaking at age 60–69 years. Rates of severe ADEs increased in older age groups. Drugs commonly associated with ADEs tended to be those primarily used for mental health and pain treatment in younger patients and those used to address chronic disease states in older patients.

Keywords: adverse drug events, geriatric population, adverse event reporting

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Drug-related misadventures in the elderly are frequently encountered across healthcare settings.[1-3] Although definitions and the use of terms to categorize harms are not homogenous across the literature, these are often catalogued as being (1) an adverse drug reaction (ADR), caused by a drug when it is used as intended or (2) within the broader category of an adverse drug event (ADE), coincident with any use (or in some case, misuse) of a drug.[4] For the sake of comparison, ADEs and ADRs are considered the same for this analysis and will be referred to as ADEs except where the cited study specified ADR. A systemic review of 14 hospital-based studies conducted across multiple countries suggested that ADR prevalence ranged widely, from about 6% to 46% (median, 11%), often depending on how ADEs were defined and detected[5]; moreover, available studies suggest that the elderly have ADEs or ADRs at a rate well above those of younger ages. For example, Budnitz and colleagues[6] looked at emergency department (ED) visits and estimated the annual rates of ADEs (excluding purposeful misuse), finding that patients age 65 years or older were

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almost 2.5 times more likely to experience an ADE leading to an ED visit and were about 1.5 times more likely to require hospitalization due to an ADE than their younger counterparts. In the ambulatory care setting, Gurwitz and colleagues[1] noted that ADEs in older persons were common (and often preventable), with an overall incidence rate of about 50 per 1000 person-years; of these, nearly 40% were considered severe.

There are various explanations posited for the observed higher rates of ADEs in older populations, such as the elderly having more comorbidities, greater frailty, and using more medications, as well as having increased risks due to altered drug metabolism, distribution, and excretion.[2,5] Polypharmacy, for example, may increase the risks of ADEs due not only to direct exposure to drugs but also to a greater propensity for drug interactions and age-related body changes; these in turn may confer less tolerance for adverse effects, should such occur. Yet, while increasing age is often considered to be directly correlated with more adverse events, not all studies show a linear association, especially across an ambulatory population. One study from the United Kingdom, using data from 48 cohort studies, noted that the age range for suspected ADRs to newly marketed drugs peaked at 50–59 years for men and at 30–39 years for women, supporting a nonlinear association.[7]

While it is possible that overall ADEs have a somewhat different age distribution than more severe adverse clinical events, there is little information investigating ADEs across age ranges by incidenc, severity, and associated causative agents. Thus, as part of an ongoing national quality-improvement effort, we conducted a comprehensive ADE data assessment from the U.S. Department of Veterans Affairs (VA), a large integrated national healthcare system. In doing so, we utilized the VA's adverse event reporting and tracking system to provide a more robust picture of these issues in the VA population.

KEY POINTS

- Retrospective database review of 484,351 adverse drug events (ADEs) in veterans revealed that the highest reporting rate occurred among patients age 60–69 years, which is contrary to common presumptions that older patients experience more ADEs.
- Older patients had a higher rate of severe ADEs compared with younger patients.
- ADE reporting may not follow a linear pattern of increasing reports in parallel with increasing age.

Methods

The VA Adverse Drug Event Reporting System (VA ADERS) is a Web-based reporting system used to centralize adverse event data for observed (or new) reactions in VA patients. This surveillance database is composed of ADEs submitted by reporters at individual VA care facilities. Adverse events are manually entered into the database at all of the 147 VA healthcare facilities. The reporting system is accessible at all levels throughout VA at all care facilities: 146 stations and the Consolidated Mail Out Pharmacy. The 146 stations include the parent facility, outpatient clinics aligned with that facility, and the community-based outpatient clinics and then are automatically coded using the Medical Dictionary for Regulatory Affairs (version 19.1 or newer).[a] Included in the VA ADERS database are ADEs that may be preventable (e.g., due to medication errors), so the database most closely resembles an ADE reporting and tracking system. The VA ADERS database is a subset of the larger set of all adverse events entered at VA facilities into the VA electronic record, called the Computerized Patient Record System (CPRS). In CPRS, the Adverse Reaction Tracking (ART) package records, via provider input, allergy and adverse reactions categorized as either observed (new) or historical (old) and hence represents the larger universe of reactions encountered (and reported) in day-to-day care and serves as the operational data for checking prescribing orders. VA ADERS operates in parallel with the operational ADE reporting in the ART package. The ART database receives over 50,000 reports each month. As reported by Emmendorfer et al.,[8] the smaller VA ADERS database houses mostly "observed" adverse reactions, reported in much greater detail than records in the ART, including those submitted to the Food and Drug Administraiton (FDA). VA ADERS includes both inpatient and outpatient ADEs (over 4,000 reports per month).

For the current evaluation, reported ADEs for 2009 through 2016 were aggregated by fiscal year (FY; October 1 through September 30). Patients were initially stratified across 9 age groups: <20, 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, 80–89, and ≥90 years. To provide a standard comparison value when tracking and trending ADE reporting, we used a denominator of the number of veterans receiving VA pharmacy benefits (at least 1 outpatient prescription) during the year, within age groups. This yielded the number of ADEs per 10,000 unique patients within each age group receiving a prescription for FYs 2009 through 2016. The number of patient prescriptions per year was evaluated based on the average number of prescriptions patients received yearly in each of the age groups.

To assess severity, we used percentages of those reports marked as severe among all reports (options include mild, moderate, and severe). Event severity is defined in the VA ADERS Web-based report template as mild (i.e., the event required minimal therapeutic intervention, such as discontiung the drug), moderate (i.e., the event required active treatment or further assessment of a nonserious outcome), or severe (e.g., a fatal outcome, life- or organ-threatening event, permanent disability or impairment or required/prolonged hospitalization). We also looked at the top 20 ADEs by primary suspect drug reported (per each age group) by volume submitted and then also the 20 drugs having the highest number of severe events reported per age group.

As this was a quality-improvement project within the VA pharmacy benefit management system, institutional review board approval was not necessary.

Results

Overall, in FYs 2009 through 2016 (inclusive), a total of 484,351 ADE reports (from 395,703 patients) were submitted by reporters from 147 facilities to the VA ADERS database. Patients were predominantly male (91%), and the mean age was 64 years. The percentage of severe ADEs was 4.6%. The majority of reports described outpatient events (83%). Overall, this represented a mean yearly report total of approximately 60,500, which equates to a report rate of 125 adverse events per 10,000 VA patients who receive at least 1 outpatient prescription annually. All age groups had adverse events reported, though the youngest (<20 years) had comparatively low numbers (114 reports) and inconsistent report totals and was excluded from the analysis. The highest yearly mean number of prescription medications used per patient was 15.4 and was found in 2 age groups: 50–59 and 60–69 years. For other age groups, the yearly mean numbers of prescription medications used per patient were as follows: 8.8 for age 20–29 years, 11.0 for age 30–39 years, 13.5 for age 40–49 years, 13.5 for age 70–79 years, 13.0 for age 80–89 years, and 12.9 for age 90 years or older.

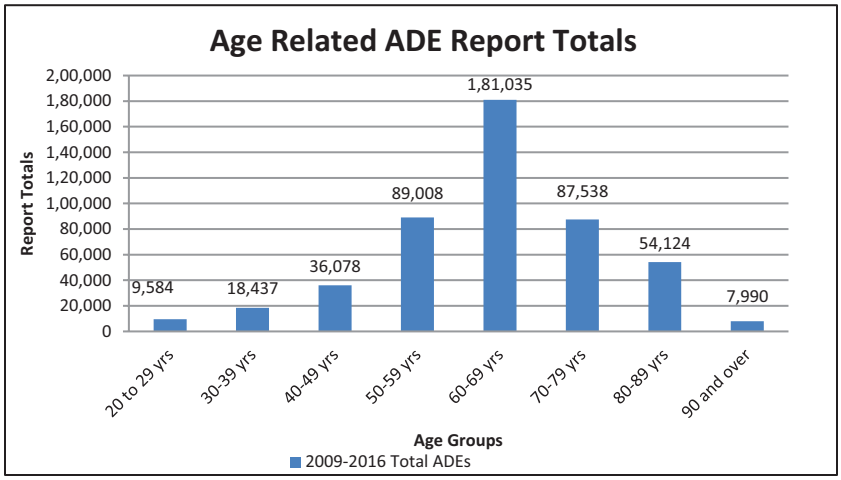
Figure 1 shows the overall number of reports by age group for the time period assessed. The raw totals increased dramatically up to patients age 60–69 year and then dropped noticeably thereafter to less than half that total for all other individual age groups.

Figure 2 normalizes the data to illustrate the mean report rates per 10,000 patients who received at least 1 outpatient prescription over the 8-year period, ranging from 68.9 for patients age 20–29 years to 148.6 for patients age 60–69 years. Figure 3 breaks the data down by year to show that the pattern remained consistent over the reporting time frame. As can be seen in both Figure 2 and Figure 3, reporting rates were nonlinear and peaked in patients age 60–69 years. Figure 3 also shows an overall decline in report total over the span of years (60,014 in FY 2009, 70,317 in FY 2010, and 50,952 in FY 2016).

On the other hand, the frequency of severe reports (of the total mild, moderate, and severe reports) increased with age after being relatively flat (about 3%) for the youngest 3 age groups, with the highest frequency in the oldest age groups (6.0% in those age 90 years or older) (Figure 4).

The types of medication most associated with ADEs differed over age groups, with the younger age groups more commonly having adverse events from mental health and pain medications, while the older age groups tended to cluster around medications for common chronic diseases (Table 1). This pattern changed to some degree when examining reports submitted with a severe outcome (Table 2), where with a few notable exceptions, mental health and pain medications (e.g., tramadol, gabapentin, antidepressants) were common in the younger age groups and medications associated with chronic disease treatment or management (e.g., lisinopril, cholesterol-lowering drugs, warfarin, terazosin) were common in the older age groups. For example, sulfamethoxazole–trimethoprim was reported with varying frequency but was commonly observed among the top 4 drugs for severe reports starting with age 30–39 years or older, and piperacillin–tazobactam was seen among multiple age groups. Opioids of various types appeared across the spectrum of age. Warfarin and other anticoagulants had an increasing presence in severe adverse events starting at age 40 years. The most reported drug across all age groups, regardless of severity, was lisinopril, which ranked first or second in all age groups except for patients age 20–29 years. Lisinopril was second to warfarin in severe reports for the three groups older than 69 years.

Figure 1. Total numbers of reported adverse drug events for combined fiscal years (FYs) 2009–16 for patients in various age groups.



Discussion

Spontaneous ADE databases, such as VA ADERS and the FDA Adverse Event Reporting System, remain cornerstones for medication safety evaluations. We used a passive reporting mechanism to assess ADEs by age, medication type, and severity over time. We observed that older patients in the VA do not experience ADEs at a greater rate when compared with all groups of younger patients (Figures 1–3). This differs from we had expected on the basis of elderly populations exhibiting greater medication use and age-related changes.

Although our findings contradict conventional wisdom, others have observed this as well. Martin et al.[7] reviewed newly marketed drugs and reported a nonlinear relationship between ADEs and

Figure 2. Rates of reported adverse drug events (events per 10,000 unique patients) for combined fiscal years (FYs) 2009–16 for patients in various age groups.

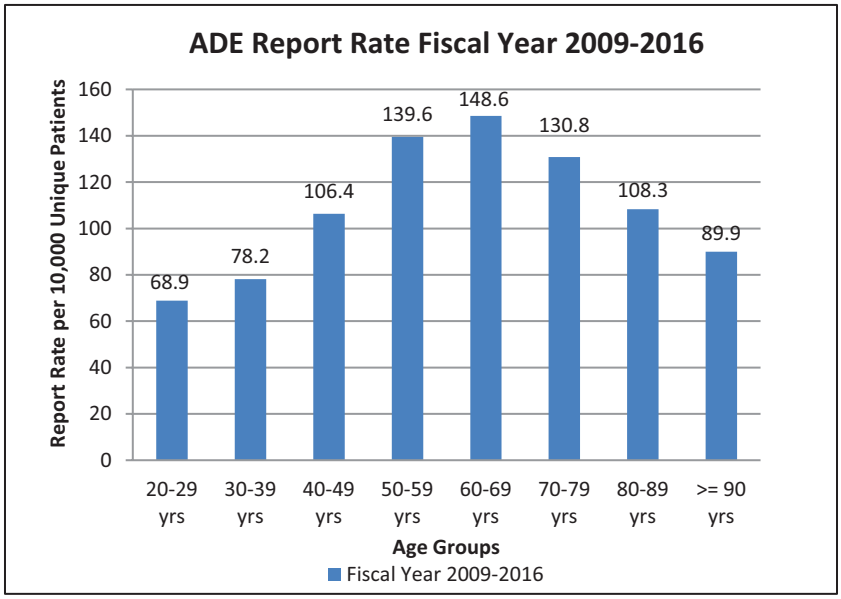
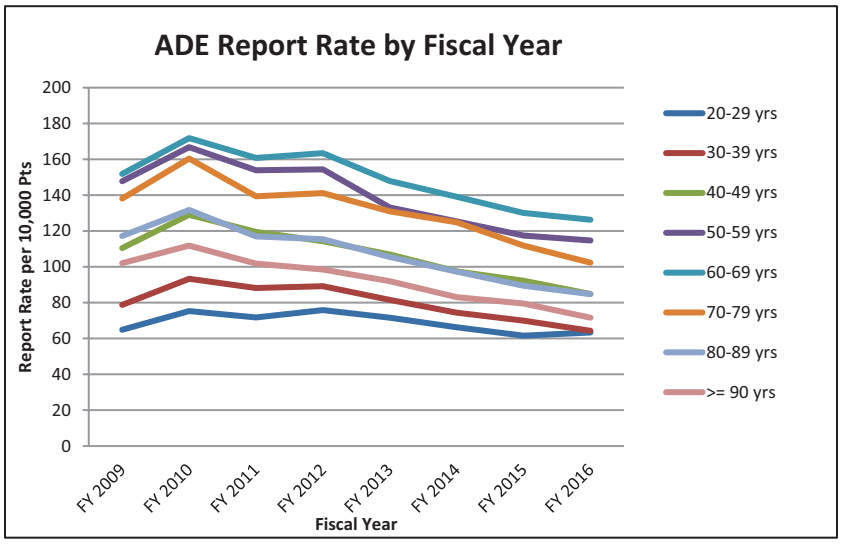


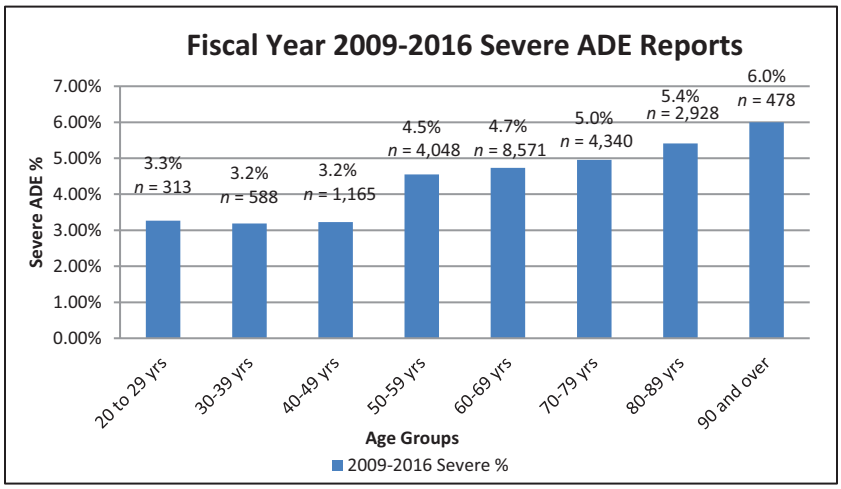
Figure 3. Changes over fiscal years (FYs) 2009–16 in rates of reported adverse drug events (events per 10,000 unique patients) for patients in various age groups.



age; for men, the highest rate was found in those 50–59 years old; in women, the highest rate was found in those 30–39 years old. We did not isolate sex in our evaluation, given the low percentage of women under VA care. We did review inpatient ADEs and found that eliminating the inpatient reports from the analysis did not change the age pattern, but report totals were lower (data not shown). In addition, the inpatient ADE report rate showed greater variability, with the mean report rate in patients age 70–79 and 80–89 years (164 and 163 per 10,000 patients, respectively), surpassing the rate in younger cohorts before declining again in patients age 90 years or older. That said, since our patient population is contiguous across inpatient and outpatient settings, we felt it more appropriate to combine them. Interestingly, while the volume of ADEs was not linearly correlated with age, our findings also align with those of Budnitz et al.,[9] who reported a higher age-related frequency of serious ADEs in ED visits, and with Shehab et al.,[10] who found the highest age-related hospitalization rates from adverse reactions in older adults. Those reports, combined with our findings, suggest that while there might be fewer ADEs among the elderly (80–89 years) and very elderly (≥90 years), when an adverse event occurs it is more likely to be severe. Finally, a recent study by Sonawane et al.[11] also suggested an escalation in severe ADE reports with increasing age. Those investigators, however, used 4 broader age groupings and found that the highest rate of severe ADEs occurred in patients age 45–64 years rather than in patients age 65 years or older. Their findings may better reflect what occurs in the population at large or may reflect variations in cohorts or differences in reporting sources (i.e., VA healthcare providers versus healthcare providers, consumers, and manufacturers in the FDA's database) and/or severity assessments. Nonetheless, their findings were not vastly different from ours, with older individuals having more severe ADEs reported than younger patients.

There are several possibilities to account for our seemingly disparate findings of a lower incidence but more severe events in old (80–89 years) and very old patients (≥90 years). The first is that the findings are accurate and there is a distinct biological reason for older patients to have a lower observed ADE rate than younger cohorts. Among a large population, those who live to older ages may constitute, at least in part, a healthy age cohort with less comorbidity and taking fewer drugs, compared with sicker, albeit younger cohorts. To assess this further, we looked at the mean number of prescription medications in each age group and found that

Figure 4. Reported severe adverse drug events for combined fiscal years 2009–16 for patients in various age groups.



the peak (about 15 medications) was in patients age 50–59 and 60–69 years over the 8 years reviewed. This trend followed the trend observed with ADE report rate by age groups with younger (<50 years) and older (≥70 years) patients receiving fewer medications. Patients at least 70 years old received about 2 fewer prescription medications annually than those patients in the groups spanning ages 50–69 years. A corollary to the above is that older age individuals may also be on stable medication regimens consisting of medications these patients have tolerated well throughout their course of treatment. Younger patients with newly diagnosed diseases and conditions may experience more adverse reactions or events as medications are initiated or titrated. Even so, age does confer negative effects to physical and mental status and even among a healthy age cohort, negative effects do occur. Thus, it is equally not surprising that the elderly may have worse outcomes if an ADE happens. This may also factor into prescriber decision-making, as less-aggressive targets and treatments are considered to avoid harm in older patients, yet even commonly used medications such as lisinopril may produce larger quantities of overall and severe ADEs in older patients.

The decrease in yearly ADE reporting during the full time period was not a focus of this study. The consistent trend of reporting rates by age groups—with respect to highest report rate per age group by year—did not change even as report totals decreased over the time frame. Reporting remained steady with roughly 50,000 ADE reports annually, and no individual age group showed an increase or a decrease with greater variability. The largest patient population counts by age groups on a yearly basis were consistently (from largest to smallest) 60–69, 70–79, 50–59, 80–89, 40–49, and 30–39 years, and the last 2 groups were comparable with the ranking for patients age 20–29 years and those age 90 years or older in FYs 2008–10, with patients age 90 years or older ranking above those age 20–29 years in FYs 2011–16.

A second possibility is that our findings may represent unknown artifactual or confounding factors that may appear to lead to higher ADE reporting in younger cohorts. One factor could hypothetically be that there is inconsistent reporting of ADEs across age groups. For example, chemotherapy drugs are frequently associated with ADEs, and these drugs are more likely to be used in older populations, where cancer is more prevalent. Only a small proportion of events in our database were attributed to chemotherapy (approximately 1% per year, or about 600 reports), so it is possible that we missed such reports since many expected ADEs (e.g., cytopenias, neutropenia-associated infections) are likely to be underreported.

A third consideration is that patients may seek care outside of the VA system. As a result, ADE reporting in patients older than 65 yearss could decrease if patients begin using Medicare and thus their ADEs occur outside VA. This would likely be seen as a rather abrupt drop in medication use in our system or an abrupt drop observed in ADEs entered into the electronic health record (ART database). However, when examining data from the ART database that should encompass all reports, we found no sudden decrease in ADEs but rather a peak in patients in their mid-60s and then a progressive decline in reports over time; we also did not see a demonstrable shift in the historical and observed mix. Of note, reporting into the ART database is commonly performed by diverse healthcare providers (e.g., physicians, pharmacists, nurses) during patient encounters and serve to trigger operational prescribing order checks. We expect that clinicians are familiar with this through training and clinical experience. The majority of reports in VA ADERS, however, are submitted by designated, trained pharmacists (about 90% annually) for the purpose of ADE tracking and trending. ADE reporting is reinforced with annual training available to interested staff, especially targeting new staff. This training focuses on what should be reported in VA ADERS, the various definitions previously mentioned and recognizing ADEs as they occur.

In addition, clinicians are trained by the medical centers on reporting allergies and adverse reactions in the electronic health record (specifically in the ART package). Moreover, with regard to prescriptions, we found a consistent pattern of average prescriptions per patient across age groups, again suggesting no abrupt change. That said, we cannot be certain that a shift toward private care might not account for some magnitude of our non-linear incidence; although we would surmise that this would also have affected severity percentages as well–yet that was not seen.

Table 1. Top 20 Drugs Reported to VA ADERS as the Primary Suspect Drug, by Age Group

	Patient Age Group							
Rank	**20–29 yr**	**30–39 yr**	**40–49 yr**	**50–59 yr**	**60–69 yr**	**70–79 yr**	**80–89 yr**	**≥90 yr**
1	Tramadol	Lisinopril	Lisinopril	Lisinopril	Lisinopril	Lisinopril	Lisinopril	Lisinopril
2	Bupropion	Bupropion	Simvastatin	Simvastatin	Simvastatin	Simvastatin	Simvastatin	Terazosin
3	Sertraline	Gabapentin	Gabapentin	Gabapentin	Atorvastatin	Atorvastatin	Terazosin	Warfarin
4	SMX–TMP	SMX–TMP	Metformin	Atorvastatin	Pravastatin	Terazosin	Warfarin	SMX–TMP
5	Trazodone	Tramadol	SMX–TMP	Metformin	Metformin	Pravastatin	Atorvastatin	Simvastatin
6	Gabapentin	Sertraline	Atorvastatin	Pravastatin	Rosuvastatin	Warfarin	Pravastatin	Donepezil
7	Venlafaxine	Venlafaxine	Tramadol	SMX–TMP	Gabapentin	Rosuvastatin	SMX–TMP	Amlodipine
8	Citalopram	Simvastatin	Pravastatin	HCTZ	Amlodipine	Metformin	Amlodipine	Ciprofloxacin
9	Morphine	Trazodone	Bupropion	Amlodipine	Terazosin	Amlodipine	HCTZ	Tramadol
10	Vancomycin	Lamotrigine	Morphine	Morphine	HCTZ	HCTZ	Donepezil	Tamsulosin
11	Risperidone	Morphine	HCTZ–lisinopril	Rosuvastatin	SMX–TMP	SMX–TMP	Gabapentin	HCTZ
12	Lamotrigine	Citalopram	HCTZ	HCTZ–lisinopril	Warfarin	Gabapentin	Rosuvastatin	Gabapentin
13	Zolpidem	Topiramate	Amlodipine	Tramadol	HCTZ–lisinopril	Morphine	Oxybutynin	Metoprolol
14	ACET–HYDR	ACET–HYDR	Venlafaxine	Bupropion	Morphine	Ciprofloxacin	Metformin	Oxybutynin
15	Prazosin	Metformin	Sertraline	Warfarin	Tramadol	HCTZ–lisinopril	Ciprofloxacin	Galantamine
16	Divalproex	Zolpidem	Trazodone	Terazosin	Spironolactone	Metoprolol	Metoprolol	Morphine
17	Haloperidol	Prazosin	ACET–HYDR	Venlafaxine	Ciprofloxacin	Spironolactone	Morphine	Atorvastatin
18	Fluoxetine	Mirtazapine	Lamotrigine	Trazodone	Bupropion	Tramadol	Tramadol	Pravastatin
19	Mirtazapine	Quetiapine	Rosuvastatin	ACET–HYDR	Losartan	Losartan	Galantamine	Mirtazapine
20	Amoxicillin	Flunisolide	Flunisolide	Ciprofloxacin	Metoprolol	Oxybutynin	Tamsulosin	Levofloxacin

[a] VA ADERS = U.S. Department of Veterans Affairs Adverse Drug Event Reporting System, SMX–TMP = sulfamethoxazole–trimethoprim, HCTZ = hydrochlorothiazide, ACET–HYDR = acetaminophen–hydrocodone.

Table 2. Top 20 Drugs from Severe Reports Reported to VA ADERS as the Primary Suspect Drug, by Age Group

	Patient Age Group							
Rank	**20–29 yr**	**30–39 yr**	**40–49 yr**	**50–59 yr**	**60–69 yr**	**70–79 yr**	**80–89 yr**	**≥90 yr**
1	Tramadol	Lisinopril	Lisinopril	Lisinopril	Lisinopril	Warfarin	Warfarin	Warfarin
2	Ibuprofen	SMX–TMP	Warfarin	Warfarin	Warfarin	Lisinopril	Lisinopril	Lisinopril
3	Bupropion	Tramadol	SMX–TMP	HCTZ–lisinopril	SMX–TMP	SMX–TMP	SMX–TMP	SMX–TMP
4	Sertraline	Trazodone	HCTZ–lisinopril	SMX–TMP	Heparin	Heparin	Simvastatin	Aspirin
5	Trazodone	Warfarin	Trazodone	Vancomycin	HCTZ–lisonopril	Simvastatin	Heparin	Simvastatin
6	Divalproex	Bupropion	Vancomycin	Simvastatin	Simvastatin	Enoxaparin	Clopidogrel	Clopidogrel
7	Vancomycin	Ibuprofen	Ibuprofen	Heparin	Vancomycin	Clopidogrel	Dabigatran	Furosemide
8	PIP–TAZ	Lamotrigine	Tramadol	Ibuprofen	Enoxaparin	Aspirin	Metoprolol	Metoprolol
9	Varenicline	Naproxen	Lithium	Naproxen	Morphine	Dabigatran	Enoxaparin	Heparin
10	Haloperidol	Sertraline	Morphine	Morphine	Ibuprofen	Vancomycin	Aspirin	Glipizide
11	Lamotrigine	Varenicline	Naproxen	Trazodone	Clopidogrel	Naproxen	Ciprofloxacin	Dabigatran
12	Clindamycin	HCTZ–lisinopril	Varenicline	Lithium	Naproxen	Metoprolol	Rivaroxaban	Digoxin
13	Warfarin	Haloperidol	Ciprofloxacin	HCTZ	PIP–TAZ	Morphine	Digoxin	Ceftriaxone
14	Pneum vac[e]	Carbamazepine	Bupropion	PIP–TAZ	Aspirin	Amiodarone	Terazosin	HCTZ
15	Quetiapine	Vancomycin	Divalproex	Enoxaparin	HCTZ	PIP–TAZ	Vancomycin	Terazosin
16	Risperidone	Topiramate	Zolpidem	Tramadol	Atorvastatin	Ibuprofen	Amiodarone	Vancomycin
17	Oxycodone	Methadone	Venlafaxine	Bupropion	Metoprolol	Rivaroxaban	Morphine	ACET–HYDR
18	Olanzapine	Ketorolac	Simvastatin	Metoprolol	Insulin	HCTZ–lisinopril	Furosemide	Donepezil
19	Sumatriptan	Divalproex	Ketorolac	Insulin	Amiodarone	HCTZ	HCTZ	Morphine
20	ACET, aripiprazole, ketorolac, fluoxetine	Zolpidem, penicillin	Heparin	Clopidogrel, losartan, aspirin, divalproex	Ciprofloxacin	Ciprofloxacin	Apixaban, atenolol	Enoxaparin, apixaban, naproxen, rivaroxaban

[a] VA ADERS = U.S. Department of Veterans Affairs Adverse Drug Event Reporting System, SMX–TMP = sulfamethoxazole–trimethoprim, HCTZ = hydrochlorothiazide, PIP–TAZ = piperacillin–tazobactam, ACET–HYDR = acetaminophen–hydrocodone.

As would be expected, we found that the type of drugs commonly associated with ADEs differed by age groups. In younger patients (i.e., 20–29 years), drugs associated with ADEs were predominantly oriented toward mental health and pain treatments, with a shift toward drugs more coincident with chronic diseases in patients age 60–69 years. While other investigators have previously focused on this issue across age groups or on selected different age groups,[1,6,9,10-12] we evaluated a large spectrum of age ranges previously unreported. Iinterestingly, some drugs (e.g., tramadol, trazodone, sulfamethoxazole–trimethoprim) appeared across multiple age groups. Budnitz and colleagues[9] found that frequent culprits correlating with emergency hospitalizations in older adults included warfarin, insulins, oral antiplatelet agents, and oral diabetes agents. We too found that anticoagulants and oral antiplatelet agents were often associated with severe outcomes in those age 60 years or older; diabetes medications appeared somewhat more sporadically across age groups and were not consistently associated with severe negative outcomes.

There were certain limitations to our evaluation. Most importantly, we used a passive reporting database that is not expected to contain all adverse events. Second, our findings within VA represent the VA patient population, which may differ from other healthcare organizations. Third, ADEs within VA reflect the patterns of drugs used frequently across our population and may not reflect drug utilization patterns outside VA. Fourth, we do not know how our clinicians and pharmacists compare with those outside VA in reporting adverse events. Perhaps different reporting rates would also lead to different findings across age groups. Finally, ADEs occurring outside the VA are not consistently entered into our database, and even if entered, are usually documented as a historical event and as such may not be captured by VA ADERS. That said, our assessment includes almost one-half million reports and to our knowledge represents the first large, national, comprehensive report of ADE by age groups.

This quality-improvement effort to review ADE reports from the large national VA healthcare system adds to the understanding of adverse drugs events by age groups and by severity and drug class. We found a nonlinear relationship between age and ADEs peaking at age 60–69 years, though rates of severe ADEs increased in older age groups. This suggests that though there may be fewer reported ADEs in the old and very old, these events, when they do occur, may be causing more harm. The top drugs associated with ADEs shifted as age patient age increased, from those primarily used for mental health and pain treatment to those used to address chronic diseases.

Conclusion

An analysis of VA ADE reports revealed a nonlinear relationship between age and events, with events peaking at age 60–69 years. Rates of severe ADEs increased in older age groups. Drugs commonly associated with ADEs tended to be those primarily used for mental health and pain treatment in younger patients and those used to address chronic disease states in older patients.

Disclosures

The authors have declared no potential conflicts of interest.

Additional information

The views expressed in this paper are those of the authors, and no official endorsement by the Department of Veterans Affairs or the United States Government is intended or should be inferred.

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