Opioids and Other Central Nervous System–Active Polypharmacy in Older Adults in the United States

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OBJECTIVES: To determine patterns of and trends in contributions to central nervous system (CNS) polypharmacy, defined by the Beers Criteria as three or more CNS-active medications of each medication class, of adults aged 65 and older seen in U.S. outpatient medical practices.

DESIGN: National Ambulatory Medical Care Survey (2004–2013).

SETTING: U.S. outpatient medical care.

PARTICIPANTS: Visits by older adults to outpatient physicians (N = 97,910).

MEASUREMENTS: Visits including three or more CNS medications including antipsychotics, benzodiazepines, nonbenzodiazepine benzodiazepine receptor agonist hypnotics (NBRAs), tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and opioids. The proportion of CNS polypharmacy that each medication class contributed during 2011 to 2013 was determined, and then logistic regression was used to determine trends from 2004 to 2013 in the contribution of individual medication classes to such polypharmacy.

RESULTS: Of recent CNS polypharmacy visits, 76.2% included an opioid, and 61.8% included a benzodiazepine; 66.0% of the polypharmacy visits with benzodiazepines included opioids, and 53.3% of the polypharmacy visits with opioids included benzodiazepines. Between 2011 and 2013, opioid and benzodiazepine co-prescribing occurred at approximately 1.50 million visits (95% confidence interval (CI) = 1.23–1.78 million) annually. From 2004 (reference) to 2013, the proportion of polypharmacy visits with opioids rose from 69.6% to 76.2% (adjusted odds ratio = 2.15, 95% CI = 1.19–3.91, $P = .01$), and the corresponding proportion that included benzodiazepines fell. Of the polypharmacy visits, the odds of SSRI, NBRA, and antipsychotic use were unchanged, and that of TCAs decreased.

CONCLUSION: In older adults, opioid use appears to be largely driving the recent national increase in CNS polypharmacy. Although concomitant use of opioids and benzodiazepines is associated with greater mortality, they are the most common contributors to CNS polypharmacy in older adults. **J Am Geriatr Soc 65:2052–2056, 2017.**

Key words: polypharmacy; opioids; benzodiazepines

When the Beers Criteria for potentially inappropriate medication use in elderly adults were first introduced 20 years ago, a select number of psychotropic medications were included, primarily because of their sedating effects: long-acting benzodiazepines, short-acting benzodiazepines above a low dosage, amitriptyline, and doxepin.[1] With each subsequent revision of the criteria, the list of psychotropic medications has grown, along with the evidence of associated risks[2–5]; the 2015 version now includes virtually every class of psychotropic medication.[6] The potential harms for older adults are particularly troubling given growing evidence that a significant proportion of psychotropic prescribing in older adults occurs in the absence of significant psychiatric symptoms[7] or a clearly defined mental health disorder.[8,9]

As the number of psychotropic medications in the Beers Criteria increased, opioids were not featured prominently, but their use is now included as potentially inappropriate in a measure of central nervous system (CNS) polypharmacy, defined as three or more prescriptions from the following classes: antipsychotics, benzodiazepines, nonbenzodiazepine benzodiazepine receptor agonist hypnotics (NBRAs), tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and opioids.[6] This revision follows evidence that CNS polypharmacy (opioids included) is associated with risk of falls[5] and cognitive decline.[10] In light of the opioid epidemic, there is now

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even greater attention focused on combined use of CNS medications. Co-prescribing of opioids and benzodiazepines is a particular cause for concern given their common role together in pharmaceutical overdose deaths. The risk of mortality increases with the dose of benzodiazepine prescribed.[11] The U.S. Food and Drug Administration (FDA) recently issued a black box warning advising of slowed breathing and death caused by co-prescribing opioids with CNS depressants, including benzodiazepines, NBRAs, and antipsychotics,[12] all of which are included in the Beers polypharmacy measure.

The use of individual psychotropic medication classes and prescription opioids has increased in older adults in the United States,[13,14] with CNS polypharmacy visits for older adults more than doubling between 2004–06 and 2011–13.[15] Although polypharmacy has risen overall, it is unclear which specific medication classes account for this growth. To address CNS polypharmacy, it is important to understand which medications and medication combinations are most common. The present study used data from the National Ambulatory Medical Care Survey (NAMCS), a nationally representative survey of visits to office-based physicians in the United States, to better characterize the relative contribution of specific medication classes to CNS polypharmacy and how this has changed over time.

METHODS

Sample

The analysis used data from NAMCS from 2004 through 2013, the most recent year available. NAMCS is a national probability sample survey of office-based and community health center–based physicians conducted annually and designed to "provide objective, reliable information about the provision and use of ambulatory medical care services in the United States".[16] Non-federally employed physicians engaged in office-based practice are sampled from the American Medical Association and American Osteopathic Association master files; physicians in anesthesiology, pathology, and radiology are excluded.

Throughout the year, each participating physician is assigned a 1-week reporting period, with data collected from a random sample of visits during that week. For very small practices, every visit may be included; for large practices, 10% of visits may be included.[17] Encounters such as house calls or in institutional settings (e.g., nursing homes) are not included. For survey years before 2012, physicians, their office staff, or field representatives of the U.S. Census Bureau recorded data for selected visits on a standardized form. Beginning in 2012, NAMCS implemented computer-assisted data collection, which Census staff primarily performed. The 2013 NAMCS public use data file does not include visits to community health centers, so such visits from other years were excluded from analysis, as NAMCS recommends. Additional technical information concerning the survey sampling design and nonresponse adjustment is provided elsewhere.[17] The current analysis was drawn from visits of individuals aged 65 and older to all outpatient providers (N = 97,910).

Medications and Other Visit Characteristics

Survey data included up to eight medications prescribed, ordered, supplied, administered, or continued during each visit. Although the 2012 and 2013 surveys included up to 10 medications, this analysis used only the first eight listed medications to be consistent across all years. The 2015 American Geriatrics Society Beers Criteria includes use of three or more CNS medication classes as potentially inappropriate: antipsychotics, benzodiazepines, NBRAs, TCAs, SSRIs, and opioids. Medications in NAMCS are assigned to therapeutic classes according to Lexicon Plus, a proprietary database of Cerner Multum, Inc.[17] A visit was classified as meeting the Beers CNS polypharmacy criteria if it included three or more medications from any of these classes.

For this analysis, basic demographic data collected, such as patient age, sex, and race and ethnicity were also included. NAMCS classifies physicians into 15 specialty groups; this analysis includes visits to all physicians, categorized as family medicine, internal medicine, psychiatry, or other medical specialties.

Statistical Methods

Survey years (2004–06, 2007–10, 2011–13) were grouped as NAMCS recommends to produce more-reliable annual visit rate estimates.[18] All analyses were completed using survey design elements for visit weight, clustering within physician practice, and stratification to allow national inferences.[17] First, all older adult visits across the study period were compared according to basic demographic and visit characteristics using difference in proportion tests. Next, the relative contribution of each medication class to CNS polypharmacy overall was determined for the most-recent time period (2011–13). Finally, the contribution of these medication classes to CNS polypharmacy during each time period was determined, and logistic regression was used to determine how odds of use for each class changed over time. For example, an odds ratio of 2.0 means that a visit in 2013 had twice the odds of that medication class contributing to CNS polypharmacy visits of a visit in 2004. Regression models were adjusted for age, sex, and race and ethnicity. Because the Beers polypharmacy measure does not include diagnosis-based exclusions, the analyses were not adjusted for clinical diagnosis. Analyses were conducted in Stata version 13.1 (Stata Corp., College Station, TX) using two-sided tests with $\alpha = .05$.

RESULTS

Background characteristics of NAMCS visits by adults aged 65 and older are presented in Table 1. During the study period, there were 97,910 office visits, 1,062 of which met criteria for CNS polypharmacy. As reported previously, between 2011 and 2013, there was polypharmacy at 1.3% of all outpatient encounters of older adults.[15] Opioids were the most commonly prescribed medication group of CNS polypharmacy encounters (76.2%), followed by benzodiazepines (61.8%) and SSRIs (51.5%) (Table 2). Although opioids and benzodiazepines

Table 1. Characteristics of Visits of Older Adults to Office-Based Physicians in the United States: 2004–2013

Characteristic	2004–06, n = 21,029	2007–10, n = 31,516	2011–13, n = 45,365	Chi-square	*P*-value
	%[a]				
Demographic					
Age					
65–74	47.8	49.7	51.2	15.88	<.001
75–84	40.1	37.1	34.7		
≥85	12.1	13.2	13.5		
Sex					
Male	41.5	42.9	43.2	4.06	.02
Female	58.6	57.1	56.8		
Race and ethnicity					
Non-Hispanic white[b]	85.6	84.2	84.9	0.91	.45
Non-Hispanic black	7.2	7.9	7.2		
Hispanic	7.2	7.9	7.9		
Diagnosis[c]					
Depression	1.7	1.8	2.1	2.45	.09
Anxiety	0.9	1.0	1.5	7.58	<.001
Insomnia	0.4	0.6	0.7	4.97	.007
Dementia	0.7	0.5	1.1	11.39	<.001
Pain	15.6	15.8	17.0	1.93	.15
Substance use disorder	0.3	0.3	0.3	0.73	.48
No mental health or pain diagnosis	80.3	80.0	78.1	3.93	.02
Provider type					
Family practice	19.6	18.1	20.9	1.70	.14
Internal medicine	21.5	22.1	19.8		
Psychiatry	1.1	1.0	1.6		
Other medical specialty	57.8	59.0	57.8		

[a]Represents the weighted percentage of visits by older adults within the time interval.
[b]Includes other race and ethnicity
[c]Diagnosis groups are not mutually exclusive (e.g., a visit of an individual with depression and pain would be represented in both diagnosis rows.

were the most-common medications in polypharmacy visits, they were also most commonly used with each other. Of individuals with CNS polypharmacy that included an opioid, 53.3% were co-prescribed a benzodiazepine; of individuals with CNS polypharmacy that included a benzodiazepine, 66.0% were co-prescribed an opioid. Between 2011 and 2013, this opioid and benzodiazepine co-prescribing occurred at approximately 1.50 million visits (95% confidence interval (CI) = 1.23–1.78 million) annually. Opioid co-prescribing was the least common of CNS polypharmacy that included an antipsychotic, just 35.9% of those prescribed an antipsychotic medication were also prescribed an opioid. Overall, TCAs were the least common class, prescribed at just 10.8% of CNS polypharmacy encounters overall and the least commonly prescribed with each other medication class.

In CNS polypharmacy encounters, opioids were the most-common medication class and the only class in which the odds of that medication class contributing to CNS polypharmacy visits increased from 2004 to 2013 (adjusted odds ratio (aOR) = 2.15, 95% CI = 1.19–3.91, $P = .01$) (Table 3). Although the odds of benzodiazepines as a polypharmacy component decreased during the study period, they were still the second-most-commonly prescribed medication group. The odds of SSRIs, NBRAs, or antipsychotics as a polypharmacy component were unchanged over the study period. TCA use decreased significantly, falling from 23.9% to 10.8% (aOR = 0.31, 95% CI = 0.15–0.66, $P = .002$).

DISCUSSION

Opioids are the most-common component of CNS polypharmacy in older adults in the United States and account for the greatest share of the overall increase in CNS polypharmacy. Although the odds of benzodiazepine use decreased slightly during the study interval, benzodiazepines remained the second-most-common polypharmacy component. Although the Beers CNS polypharmacy measure cites the risk of falls as its primary rationale, the recent FDA black box warning primarily concerns risk of respiratory suppression and death due to concomitant use of opioids and other CNS depressants, most notably benzodiazepines. More than 30% of overdose deaths of U.S. veterans related to opioids also include benzodiazepines.[19] Therefore, it is particularly troubling that opioids and benzodiazepines are the two medication groups that most contribute to CNS polypharmacy in older adults.

From 2004 to 2013, although polypharmacy grew overall, the odds of SSRIs, NBRAs, or antipsychotics as a polypharmacy component were unchanged. This is consistent with previous analyses suggesting growth of these individual medication classes.[15,20–22] Although the opioid-specific growth may be attributed to the emphasis on treatment of pain, growth of other medication classes may reflect polypharmacy used to target other specific indication (e.g., depression) or more-widespread use of medications for multiple off-label indications. For example, greater use of quetiapine may reflect indication expansion

Table 2. Patterns of Central Nervous System (CNS) Polypharmacy at Visits of Older Adults Seen in Office-Based Medical Care in the United States: 2011–2013

Medication	Opioid, n = 465	Benzodiazepine, n = 393	Selective Serotonin Reuptake Inhibitor, n = 300	Nonbenzodiazepine Benzodiazepine Receptor Agonist Hypnotic, n = 150	Antipsychotic, n = 117	Tricyclic Antidepressant, n = 87
	% (95% Confidence Interval)					
Overall, N = 618[a]	76.2 (70.8–80.9)	61.8 (56.5–66.9)	51.5 (45.7–57.2)	25.6 (20.9–31.0)	18.1 (13.7–23.7)	10.8 (8.2–14.0)
Opioid	—	66.0 (58.4–72.8)	62.8 (54.5–70.5)	64.8 (52.8–75.1)	35.9 (24.0–49.8)	61.1 (46.8–73.7)
Benzodiazepine	53.3 (47.3–59.6)	—	66.5 (59.1–73.2)	45.3 (34.7–56.5)	67.5 (53.8–78.7)	54.9 (40.8–68.3)
Selective serotonin reuptake inhibitor	42.4 (36.0–49.2)	55.3 (48.0–62.5)	—	47.7 (36.2–59.5)	54.3 (40.2–67.8)	47.4 (34.1–61.0)
Nonbenzodiazepine benzodiazepine receptor agonist hypnotic	21.8 (16.8–27.7)	18.8 (13.8–25.1)	23.8 (17.6–31.3)	—	26.3 (15.4–41.2)	18.7 (10.7–30.5)
Antipsychotic	8.5 (5.5–13.1)	19.8 (14.0–27.2)	19.1 (13.0–27.3)	18.6 (10.5–30.9)	—	13.9 (7.0–25.7)
Tricyclic antidepressant	8.6 (6.0–12.2)	9.5 (6.5–13.9)	9.9 (6.5–14.8)	7.8 (4.5–13.4)	8.2 (4.4–14.9)	—

[a]Percentage of CNS polypharmacy overall that includes a given medication class from 2011 to 2013. Within the column for each class, the rows reflect the proportion of polypharmacy within that specific class that includes the other medication groups. For example, 76.2% of CNS polypharmacy encounters overall from 2011 to 2013 included an opioid; of those on an opioid, 8.5% were also prescribed an antipsychotic. In contrast, 18.1% of CNS polypharmacy encounters overall from 2011 to 2013 included an antipsychotic; of those on an antipsychotic, 35.9% were also prescribed an opioid.

Table 3. Trends in Central Nervous System (CNS) Polypharmacy Constituent Medication Classes at Visits of Older Adults to Office-Based Physicians in the United States: 204–2013

Medication Group	Percentage of CNS Polypharmacy Visits, N = 1,062			OR[a] (95% Confidence Interval)	P-Value
	2004–06	2007–10	2011–13		
Opioid	69.6	67.5	76.2	2.15 (1.19–3.91)	.01
Benzodiazepine	68.9	78.7	61.8	0.36 (0.17–0.74)	.006
Selective serotonin reuptake inhibitor	52.5	58.5	51.5	0.63 (0.35–1.15)	.13
Nonbenzodiazepine benzodiazepine receptor agonist hypnotic	22.3	26.4	25.6	1.23 (0.67–2.27)	.51
Antipsychotic	18.6	22.5	18.1	0.88 (0.48–1.62)	.68
Tricyclic antidepressant	23.9	12.0	10.8	0.31 (0.15–0.66)	.002

[a]The odds ratio (OR) is associated with a transformed survey year variable ((survey year–2004)/9) and therefore estimates the change in odds of a visit with the particular medication class of all CNS polypharmacy visits over the entire 2004–2013 study period. For example, in 2013, the odds of a Tricyclic antidepressant contributing to CNS polypharmacy were 0.31 relative to 2004. Logistic regression models were adjusted for age, sex, and race and ethnicity.

from its FDA approval in 2009 to augment antidepressants for depression and growth in off-label use for insomnia, anxiety, or both. Over the study period, use of TCAs declined significantly. This decline may be due to greater recognition by providers of adverse effects associated with medications with high anticholinergic burden in older adults,[23] with many alternative medications with more-favorable side effects available for depression, anxiety, and neuropathy.

This study has several limitations. NAMCS does not account for whether a prescribed medication is taken regularly versus as needed, so it is possible that the extent of regular use was overestimated. Because the data were multiple cross-sectional samples, outcomes associated with medication use cannot be reported on. Because NAMCS is a survey of office-based medical practice, it does not include physicians practicing in other settings or nonphysician providers. In addition, being based on a survey of U.S. physicians, the results examine trends only in the U.S. healthcare system and do not generalize internationally. Physician nonresponse might have introduced bias into the results, but the survey weights that NAMCS designed account for this to produce unbiased national estimates.[16] Finally, in 2012, NAMCS began using Census field representatives rather than physician office staff to conduct data collection. NAMCS reports that these changes did not affect diagnosis results, although the number of medications reported decreased, for which National Center for Health Statistics (NCHS) NCHS staff "have researched ... [all] possible contributing factors" without clear explanation,[16] which suggests that the current study results may have underestimated the actual increase in CNS polypharmacy visits.

In light of the serious health consequences for older adults associated with CNS polypharmacy, potentially including falls and death, it is troubling that such prescribing continues to rise.[15] Although this combination of medications may be appropriate in select populations, use

should be considered only after careful assessment of the risks, benefits, and alternatives. Public attitudes have grown more favorable toward psychotropic medications,[24] and older adults have become more open to mental health treatment. Although this may lead to better treatment for some older adults, it may also lead to inappropriate overtreatment for others. In light of the recent FDA warning, co-prescribing of opioids and benzodiazepines is particularly troubling. It is critical to reduce this common and potentially lethal prescribing. There have been promising studies implementing structured algorithms to reduce polypharmacy, including psychotropic medications, demonstrating success in discontinuing medication without adverse effects, often with significant improvement in health outcomes.[25] Direct patient education about the harms potentially associated with medications that contribute to CNS polypharmacy may also lead some people to initiate discussions about appropriate prescribing, as demonstrated with chronic benzodiazepine use.[26] Lastly, improving access to evidence-based nonpharmacological treatments for insomnia, anxiety, or pain might also limit polypharmacy. In treatment of older adults, the adage "less is more" holds true, and further work is needed to emphasize deprescribing in older adults.

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REFERENCES

1. Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly: An update. Arch Intern Med 1997;157:1531–1536.
2. Woolcott JC, Richardson KJ, Wiens MO et al. Meta-analysis of the impact of 9 medication classes on falls in elderly persons. Arch Intern Med 2009;169:1952–1960.
3. Wang PS, Bohn RL, Glynn RJ et al. Hazardous benzodiazepine regimens in the elderly: Effects of half-life, dosage, and duration on risk of hip fracture. Am J Psychiatry 2001;158:892–898.
4. Glass J, Lanctot KL, Herrmann N et al. Sedative hypnotics in older people with insomnia: Meta-analysis of risks and benefits. BMJ 2005;331:1169.
5. Hanlon JT, Roudreau RM, Roumani YF et al. Number and dosage of central nervous system medications on recurrent falls in community elders: The Health, Aging and Body Composition study. J Gerontol A Biol Sci Med Sci 2009;64A:492–498.
6. American Geriatrics Society Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated Beers criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2015;63:2227–2246.
7. Maust DT, Mavandadi S, Eakin A et al. Telephone-based behavioral health assessment for older adults starting a new psychiatric medication. Am J Geriatr Psychiatry 2011;19:851–858.
8. Mojtabai R, Olfson M. Proportion of antidepressants prescribed without a psychiatric diagnosis is growing. Health Aff (Millwood) 2011;30:1434–1442.
9. Wiechers IR, Kirwin PD, Rosenheck RA. Increased risk among older veterans of prescribing psychotropic medication in the absence of psychiatric diagnoses. Am J Geriatr Psychiatry 2014;22:531–539.
10. Wright RM, Roumani YF, Boudreau R et al. Effect of central nervous system medication use on decline in cognition in community dwelling older adults: Findings from the Health, Aging and Body Composition Study. J Am Geriatr Soc 2009;57:243–250.
11. Park TW, Saitz R, Ganoczy D et al. Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: Case-cohort study. BMJ 2015;350:h2698.
12. FDA Drug Safety Communication: FDA Warns About Serious Risks and Death When Combining Opioid Pain and Cough Medicines with Benzodiazepines; Requires Its Strongest Warning. U.S. Food & Drug Administration [on-line]. Available at http://www.fda.gov/Drugs/DrugSafety/ucm518473.htm Accessed January 3, 2007.
13. Maust DT, Blow FC, Wiechers IR et al. National trends in antidepressant, benzodiazepine, and other sedative-hypnotic treatment of older adults in psychiatric and primary care. J Clin Psychiatry 2017; In press.
14. Olfson M, Wang S, Crystal S et al. National trends in the office-based prescription of schedule II opioids. J Clin Psychiatry 2013;74:932–939.
15. Maust DT, Gerlach LB, Gibson A et al. Trends in CNS-active polypharmacy among older adults seen in outpatient care in the United States. JAMA Intern Med 2017;177:583–585.
16. National Center for Health Statistics, Centers for Disease Control and Prevention. About the Ambulatory Health Care Surveys: National Ambulatory Medical Care Survey [on-line]. Available at http://www.cdc.gov/nchs/ahcd/about_ahcd.htm Accessed July 10, 2016.
17. National Center for Health Statistics, Centers for Disease Control and Prevention. National Ambulatory Medical Care Survey: 2013 NAMCS Micro-Data File Documentation [on-line]. Available at ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NAMCS/doc2013.pdf Accessed on July 21, 2016.
18. Hsiao CJ. Understanding and Using NAMCS and NHAMCS Data: Data Tools and Basic Programming Techniques. National Center for Health Statistics, Centers for Disease Control and Prevention [on-line]. Available at https://www.cdc.gov/nchs/ppt/nchs2010/03_hsiao.pdf Accessed on July 21, 2016.
19. Chen LH, Hedegaard H, Warner M. Drug-poisoning deaths involving opioid analgesics: United States, 1999–2011. NCHS Data Brief 2014;166:1–8.
20. Kaufmann CN, Apira AP, Alexander GC et al. Trends in prescribing of sedative-hypnotic medications in the USA: 1993–2010. Pharmacoepidemiol Drug Saf 2016;25:637–645.
21. Kaufmann CN, Spira AP, Depp CA et al. Continuing versus new prescriptions for sedative-hypnotic medications: United States, 2005–2012. Am J Public Health 2016;106:2019–2025.
22. Olfson M, Blanco C, Liu SM et al. National trends in the office-based treatment of children, adolescents, and adults with antipsychotics. Arch Gen Psychiatry 2012;69:1247–1256.
23. Campbell NL, Perkins AJ, Bradt P et al. Association of anticholinergic burden with cognitive impairment and health care utilization among a diverse ambulatory older adult population. Pharmacotherapy 2016;36:1123–1131.
24. Mojtabai R. Americans' attitudes toward psychiatric medications: 1998–2006. Psychiatr Serv 2009;60:1015–1023.
25. Garfinkel D, Mangin D. Feasibility study of a systematic approach for discontinuation of multiple medications in older adults: Addressing polypharmacy. Arch Intern Med 2010;170:1648–1654.
26. Tannenbaum C, Martin P, Tamblyn R et al. Reduction of inappropriate benzodiazepine prescriptions among older adults through direct patient education: The EMPOWER cluster randomized trial. JAMA Intern Med 2014;174:890–898.