Published in final edited form as:
J Am Geriatr Soc. 2011 September ; 59(9): 1673–1678. doi:10.1111/j.1532-5415.2011.03524.x.

Exposure to potentially harmful drug-disease interactions among older community-dwelling veterans based on the

Please address all correspondence to Mary Jo Pugh, PhD, RN, South Texas Veterans Health Care System, VERDICT REAP (11C6), 7400 Merton Minter, San Antonio, TX 78229, Phone: 210-617-5300 x17193, Fax: 210-567-4423, pughm@uthscsa.edu or maryjo.pugh2@va.gov.

An abstract presenting a portion of these data was presented at the Annual Meeting of the American Geriatrics Society in Orlando, May 2010.

Conflict of Interest Checklist: Below is the table for all authors to complete and attach to their papers during submission.

Elements of Financial/Personal Conflicts	Mary Jo Pugh		Catherine Starner		Megan Amuan		Dan R. Berlowitz		Monica Horton		Zachary Marcum		Joseph T. Hanlon	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Employment or Affiliation	X			X	X		X		X			X	X	
Grants/Funds	X			X		X	X			X		X		X
Honoraria	X			X		X		X		X		X		X
Speaker Forum		X		X		X		X		X		X		X
Consultant		X		X		X		X		X		X		X
Stocks		X		X		X		X		X		X		X
Royalties		X		X		X		X		X		X		X
Expert Testimony		X		X		X		X		X		X		X
Board Member		X		X		X		X		X		X		X
Patents		X		X		X		X		X		X		X
Personal Relationship		X		X		X		X		X		X		X

***Authors can be listed by abbreviations of their names**

For "yes", provide a brief explanation:

Authors MJP and MH are employed by the South Texas Veterans Health Care System. DRB and MEA are employed by the Edith Nourse Rogers Memorial VA Hospital and JTH is employed by the VA Pittsburgh Healthcare System. This study was funded by VA HSR&D IIR 06-062.

Dr. Pugh has received research funding from **VA HSR&D** DHI 09-237 (PI); **VA HSR&D** IIR-06-062 PI, **Epilepsy Foundation** PI, VA HSRD PPO 09-295 PI, **VA HSR&D** IIR 02-274 PI. Pugh as co-I: **VA HSR&D** IIR 08-274, **VA HSR&D** SDR-07-042, IIR-05-121, IAF-06-080, IIR-09-335, SHP 08-140, TRX 01-091 **Department of Defense** CDMRP 09090014, **NIH** R01-NR010828, Pugh Speaker Honoraria: 2009 Kelsey Seybold Research Foundation $400.

Dr Berlowitz has received funding from VA HSR&D RRP 09-112 as PI, **VA HSR&D** IIR-06-062 as Co-I.

Dr. Hanlon has received research funding from National Institute of Aging grants (R01AG027017, P30AG024827, T32 AG021885, K07AG033174, R01AG034056), a National Institute of Mental Health grant (R34 MH082682), a National Institute of Nursing Research grant (R01NR010135), an Agency for Healthcare Research and Quality grant (R01HS017695) and from **VA HSR&D** IIR-06-062.

Author Contributions:

Dr Pugh contributed to concept and design of the study, acquisition of data, analysis and interpretation of data, and preparation of manuscript.

Dr. Starner contributed to design of the study, interpretation of data, and preparation of manuscript.

Ms. Amuan contributed to acquisition of data, analysis of data, and preparation of manuscript.

Dr. Berlowitz contributed to design of the study, interpretation of data, and preparation of manuscript.

Dr. Marcum contributed to interpretation of data, and preparation of manuscript.

Dr. Horton contributed to interpretation of data, and preparation of manuscript.

Dr. Hanlon contributed to concept and design of the study, interpretation of data, and preparation of manuscript.

Healthcare Effectiveness Data and Information Set quality measure: Who is at risk?

Mary Jo V. Pugh, PhD[1,2,3], **Catherine I. Starner, PharmD**[4], **Megan E. Amuan, MPH**[5], **Dan R. Berlowitz, MD, MPH**[5,6], **Monica Horton, MD**[3,7], **Zachary A. Marcum, PharmD**[8], and **Joseph T. Hanlon, PharmD, MS**[8,9]

[1]South Texas Veterans Health Care System, VERDICT REAP

[2]University of Texas Health Science Center at San Antonio, Department of Epidemiology and Biostatistics

[3]University of Texas Health Science Center at San Antonio, Division of Geriatrics, Gerontology, and Palliative Medicine

[4]Prime Therapeutics, Minneapolis, MN

[5]Edith Nourse Rogers Memorial VA Hospital, CHQOER, Bedford, MA

[6]Boston University School of Public Health, Boston, MA

[7]South Texas Veterans Health Care System, Geriatrics and Extended Care

[8]Department of Medicine (Geriatrics), School of Medicine

[9]Department of Pharmacy and Therapeutics, School of Pharmacy, Department of Epidemiology, Graduate School of Public Health, and Clinical and Translational Science Institute, University of Pittsburgh, Pittsburgh; Center for Health Equity Research and Geriatric Research Education and Clinical Center, Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA

Abstract

Objectives—Identify prevalence and risk factors for drug-disease interactions included in the Healthcare Effectiveness Data and Information Set Drug-Disease Interaction (HEDIS Rx-DIS) Measure.

Design—Cross-sectional retrospective database analysis.

Setting—Outpatient clinics within the Department of Veterans Affairs (VA).

Participants—Individuals 65 years and older who received VA outpatient care October 1, 2003 to September 30, 2006.

Measurements—We identified drug-disease interactions in 2006 defined by the HEDIS Rx-DIS criteria among VA patients with dementia, falls, and chronic renal failure using VA pharmacy and administrative databases. We examined factors associated with HEDIS Rx-DIS exposure including demographic, health status, and access to care factors including VA outpatient health services use and co-payment status.

Results—Of the 305,041 older veterans who met criteria for inclusion, the one-year prevalence of HEDIS Rx-DIS exposure was 15.2%; prevalence was 20.2% for dementia, 16.2% for falls and 8.5% for chronic renal failure. Patients with high disease burden (physical, psychiatric, number of medications) were significantly more likely to have HEDIS Rx-DIS exposure, regardless of condition. Hispanics and individuals with no copayments were more likely to have Rx-DIS exposure than whites or those with required copayments. There was variation on other predictors based on the type of Rx-DIS.

Conclusion—The prevalence of Rx-DIS was common in older VA outpatients. Future studies should examine the risk of Rx-DIS exposure on health outcomes using separate analyses for each type of Rx-DIS separately before combining all Rx-DIS into a single measure of exposure. Studies that examine the effectiveness of interventions to reduce Rx-DIS exposure will also be helpful in improving the quality of care for older patients.

Keywords

Drug disease interaction; HEDIS measures; Potentially Inappropriate Prescribing; aged; pharmacoepidemiology

INTRODUCTION

Potentially inappropriate prescribing in the Elderly (PIPE) has been a growing concern over the past decade. While most studies have examined use of high risk drugs for the elderly (e.g., Beers criteria), concern has begun to expand to other realms of PIPE such as drug-disease interactions.[1–5] Studies have examined exposure to drug-disease interactions defined by Beers, in a variety of settings.[1,2,6,7,8–13] Previous research has shown that drug-disease interactions (i.e., medication(s) exacerbating pre-existing conditions) are common and are associated with adverse drug reactions in older adults; thus they represent an important area of inquiry.[14,15]

In fact, the National Committee on Quality Assurance (NCQA) developed a drug-disease interaction measure as part of the 2007 Healthcare Effectiveness Data and Information Set (HEDIS) quality measures (hereafter HEDIS Rx-DIS) based on an earlier measure of 28 drug-disease interactions involving 14 diseases or conditions developed by Lindblad and colleagues (e.g., peptic ulcer disease and asprin and non-asprin non-steroidal anti-inflammatory (NSAID) drugs; syncope and alpha blockers; systolic heart failure and first generation calcium channel blockers. [7] From the Lindblad measure, the NCQA expert panel reached consensus on a subset of drug-disease interactions that could be readily measured using administrative data and that were potentially associated with adverse outcomes. The three conditions and medication groups considered inappropriate for individuals with those conditions are included in the HEDIS Rx-DIS measure that is now used to monitor quality of prescribing by managed care: dementia, falls and chronic renal failure. While NCQA has published rates of HEDIS Rx-DIS in their report on the state of health care quality in 2009, [16] other studies examining Rx-DIS have used broader measures. Since the HEDIS Rx-DIS measure is a nationally accepted quality measure, we focus our assessment on the three conditions included in that measure.

The purpose of this paper is to examine the extent to which HEDIS Rx-DIS exposure occurs among older community dwelling VA patients and factors associated with that exposure. Mirroring the HEDIS Rx-DIS QI measurement we examined the prevalence of HEDIS Rx-DIS exposure overall and then by disease/ condition. In order to determine if risk factors were consistent across conditions, we also identified risk factors for HEDIS Rx-DIS exposure overall and by disease/condition.

METHODS

Data and Study Population

After Institutional Review Board approval we obtained national VA inpatient, outpatient and pharmacy data from fiscal year 2004 (FY04; October 1, 2003 to September 30, 2004) through FY06 (October 1, 2005–September 30, 2006) for individuals who were 65 or older at the beginning of FY05. We merged pharmacy and diagnostic datasets using the encrypted

identifier included in each dataset. In order to assure that we had adequate data to identify comorbid conditions and prior medication use, we selected from that population individuals who received care regularly in the VA healthcare system—having at least one outpatient or inpatient visit each year. Individuals who resided in VA community living centers (based on VA extended care file) data for all of FY2006 and those who died prior to 2006 were not included. Individuals who were admitted to a community living center during 2006 or who died after receiving care in 2006 were included. We further restricted analyses to individuals having ICD-9-CM code based diagnoses/ medications indicative of falls, dementia, or chronic renal failure as outlined by the NCQA, which required a single diagnosis.

Measures

Drug-Disease Interaction—We first identified individuals with dementia, falls, and chronic renal failure in VA inpatient and outpatient databases (FY04-FY06) using ICD-9-CM codes (and medications for dementia) identified by the NCQA.[17] For those having a diagnosis indicative of dementia, falls and chronic renal failure, or dementia medications (donezepil, galantamine, rivastigmine, tacrine, and memantine), we identified use of potentially harmful medications in FY06 (see Table 1) using the VA Product variable in the VA Pharmacy Benefits Management database.

Individuals diagnosed with dementia, falls or chronic renal failure, and who later had an order for and were dispensed medications considered relatively or potentially contraindicated in FY06, were classified as having Rx-DIS exposure for that condition. We then calculated the overall prevalence of any HEDIS-Rx-DIS among individuals who met criteria for dementia, falls or chronic renal failure, and the prevalence for individuals within each condition of interest.

Patient Demographic Characteristics—Patient demographic characteristics included age, sex, race, and marital status. Demographic characteristics were identified using VA administrative data. With the exception of race, these demographic characteristics are well documented and complete in the medical record. Because the process of recording race changed in 2002, race data are more likely to be missing than other aspects of VA administrative data. Thus, we used a process in which we looked back in VA data for previous years and forward in the data in subsequent years to fill in missing race values. Individuals with missing race data (N=44,513, 14.6% of cohort meeting inclusion criteria for quality indicators) were excluded from the analysis of risk factors for HEDIS Rx-DIS exposure since inclusion of these individuals in a separate missing category complicates interpretation of race findings, and findings were essentially the same in analyses where they were included.

Health Status Factors—Clinical characteristics included in this study included counts of a) chronic physical comorbidities, b) mental health comorbidities, and c) unique medication classes prescribed the previous year. Pre-existing comorbidities were identified between FY04-05 to assure adequate time for accurate assessment.[18] We used ICD-9-CM codes included in VA inpatient and outpatient databases to identify conditions included in the Selim Physical and Mental Comorbidity Indices (CI).[19] The Physical CI includes 30 comorbid conditions (0,1; e.g., cerebrovascular disease, diabetes, hypertension) which are counted to create a physical disease burden score ranging from 0–30. The Mental CI includes six comorbid conditions (anxiety, depression, post-traumatic stress disorder, bipolar disorder, alcohol abuse/ dependence, and schizophrenia) that are similarly summed to create a score indicating psychiatric disease burden. In our previous work we have found that creation of categorical variables assist in interpretation mental health conditions (0, 1, 2+). The Physical and Mental CI have been found to be associated with both mortality and issues

of suboptimal prescribing in previous research.[5,20] In addition to comorbid conditions, we also used a count of unique medication classes prescribed for each patient in FY05—the year prior to Rx-DIS identification. [21]

Access to Care Factors—The first variable measuring access to care was an indicator identifying those for whom pharmacy co-payments were required based on VA priority group. VA priority groups are associated with physical or mental health status and illness severity as well as socioeconomic status. As defined here, priority group status that warranted a waiver of pharmacy copayments ($8 in 2006) included veterans with a service-connected disability ≥50%, or individuals who were catastrophically disabled, very low income, or had specific war-related experiences. [22]

The second variable measuring access to care was prior receipt of geriatric care. Individuals who received care in geriatric outpatient clinics or inpatient geriatric evaluation and management in FY05 were identified as having prior geriatric care.[23] The third variable measuring access to care was a count of primary care visits. Because prior literature found that patients with many primary care visits the previous year were more likely to have an exposure to potentially inappropriate medications as measured by the Beers criteria, those with more frequent visits to primary care (5+ in a year) may be sicker, and thus at higher risk of RX-DIS exposure.[3,24] Based on prior studies and the empirical distribution we classified patients as having 0–1, 2–4 or 5+ primary care visits.

Analysis

We first provide the prevalence of HEDIS Rx-DIS overall among those meeting criteria for dementia, falls, and chronic renal failure in addition to the prevalence of HEDIS Rx-DIS exposure by specific condition. Finally, we identified risk factors for HEDIS Rx-DIS overall, and then within each condition of interest using logistic regression analysis. We conducted collinearity diagnostic testing to assure that multicollinearity did not exist among the variables included in the logistic regression models. SAS 9.1 software® (SAS Institute Inc., Cary, North Carolina) was used to perform all analyses.

RESULTS

Of the 1,780,787 older community-dwelling veterans who received care regularly within the VA each year between FY 04-06, 305,041 met criteria for dementia, falls or chronic renal failure. Table 1 shows the prevalence of drug-disease interactions by disease state/condition. Based on the HEDIS Rx-DIS criteria 46,481 (15.2%) of this cohort had one or more HEDIS Rx-DIS exposure during FY06. HEDIS Rx-DIS exposure was 20.2% among those with a history of dementia, 16.2% among those with a history of falls and 8.5% among those with a history of chronic renal failure.

Table 2 shows descriptive statistics for individuals with one or more vs. no Rx-DIS and for individuals with and without Rx-DIS exposure by condition. There were statistically significant differences between those with and without Rx-DIS exposure for all bivariate analyses except for marital status in dementia and falls, and gender in chronic renal failure. Table 3 shows adjusted odds ratios (OR) and 95% confidence intervals (CI) from logistic regression models examining the association between Rx-DIS exposure and independent variables overall and for each condition. In the overall analysis, risk factors included younger age, women, Hispanic ethnicity, psychiatric comorbidities, and higher levels of primary care utilization. There was, however, some variation when examining Rx-DIS within specific disease conditions with regard to race, gender, psychiatric comorbidity and geriatric and primary care utilization.

DISCUSSION

Our study of community dwelling VA patients is the first to report prevalence of Rx-DIS exposure and potential risk factors for exposure based on the HEDIS measure. The prevalence of Rx-DIS is similar to rates of PIPE as defined by the Beers criteria and other measures of high risk medications in the elderly (15–40%).[1,8,9,25] Given recent data showing a strong relationship between drug disease interactions and adverse drug reactions, this form of suboptimal prescribing is a serious public health concern. [14,15]

While other published studies using measures of Rx-DIS exposure that included more conditions and medications had much higher rates of exposure (Hastings, et al., 5.7% and Lindblad, et al., 15.3%)[12,13,26] in context, our data appear consistent with prior work. Overall rates of any exposure were lower than population estimates by the NCQA using Medicare data in 2006, however the differences were primarily due to lower Rx-DIS exposure among individuals with dementia and chronic renal failure.[16] Consistent with other studies examining drug-disease interactions, the number of unique medications had a very strong association with Rx-DIS exposure.[10] However, unlike the study by Zhan and colleagues, women and Hispanics (but not men or African Americans) were at greater risk of HEDIS Rx-DIS overall. These differences in demographic characteristics may be due to the restricted number of Rx-DIS included in the HEDIS measure compared to the more comprehensive measure used by Zhan and colleagues.[10]

Our study demonstrated the importance of examining both exposure and risk factors by the specific type of Rx-DIS. While rates of exposure for dementia and falls were between 15–20%, exposure for renal failure was only 8.5%, perhaps indicating more care when prescribing medications for patients with renal failure. Alternatively, our measure may underestimate exposure to NSAIDs that can be obtained over the counter since generic forms may be obtained outside the VA pharmacy system at relatively low cost.

While some risk factors were consistently associated with Rx-DIS exposure (e.g., younger age, number of unique medications, psychiatric comorbidity, exempt from copayment), we found that the relationship between certain characteristics varied by the specific Rx-DIS (e.g. race, gender, geriatric care and primary care utilization). The only race category that had consistently higher rates of Rx-DIS compared to whites was Hispanic. For African Americans, likelihood of Rx-DIS was lower than that for whites only among those with dementia; there was no significant difference for falls, and there was a slightly higher likelihood for renal failure. These findings are consistent with higher rates of PIPE in whites based on the Beers criteria,[3,25] and a broad literature identifying racial disparities in care for patients ranging from cardiac disease, hypertension, epilepsy, and mental health conditions.[32,33,34] Alternatively, examination of bivariate data by race indicated that Hispanics were more likely to have multiple mental health conditions and African Americans were more likely than whites to have arthritis which may be treated with potentially problematic medications. While the interaction effect was not statistically significant, variation in comorbidity profiles may influence Rx-DIS exposure.

Studies of PIPE based on the Beers criteria consistently find that women are at increased risk for exposure,[4,35] however our study found that women were only at higher risk for dementia Rx-DIS. Thus, it appears that higher risk for women is not comprehensive, but rather specific to dementia or the types of drugs that are problematic for dementia (e.g., anticholinergics, tricyclic antidepressants).

Interestingly geriatric care the prior year was associated with increased risk for Rx-DIS exposure overall, which is inconsistent with prior studies examining exposure to Beers criteria drugs found geriatric care reduced likelihood of exposure. [35,36] However,

examination of Rx-DIS by condition revealed reduced likelihood of dementia and renal Rx-DIS exposure, and higher likelihood of fall Rx-DIS exposure. Since fall assessment and prevention is an important component of geriatric care, it is possible that the finding results from increased screening and documentation of falls in the electronic medical record by geriatricians. Thus these data may reflect not only a selection bias, where the most complicated patients are seen by geriatricians, but also a detection bias where patients receiving care from a geriatrician are more likely to have conditions such as falls documented in the electronic medical record.

Our data have several limitations. First, they reflect only those medications and healthcare utilization received in the VA. It is possible that other medications were ordered and dispensed from outside the VA since the study period was after the initiation of Medicare Part D (January 1, 2006).[37] However, because patterns of Rx-DIS and prescribing were similar in 2004, 2005 and 2006, we believe the potential impact on our findings is limited. Second, in identifying the Rx-DIS conditions, we had access only to VA administrative data. While Medicare data may improve our ascertainment of the conditions of interest, we had two years of prior data to assess comorbid conditions, which is the recommended period to identify chronic disease states within VA data.[18] With regard to healthcare utilization, our criteria requiring at least one inpatient or outpatient visit per year may have excluded individuals who frequently receive outside care, biasing the cohort to individuals who are sicker. Examination of Rx-DIS exposure using looser inclusion criteria, but all available data since 2003, resulted in similar rates of exposure and similar risk factors.

Moreover, our study assessed Rx-DIS exposure prior to the final approval of the HEDIS Rx-DIS measure. Thus, providers were not aware of this quality measure at the time of the study. Because this measure includes many Rx-DIS described previously in the Beers and McLeod criteria, and because the selected Rx-DIS are a very small, but clinically important component of these measures, the Rx-DIS themselves or data supporting the Rx-DIS were available to clinicians for a number of years.[1,2,6,11, 38] While it is possible that publication of this measure in 2007 may have led to reductions in Rx-DIS since this measure may have had broader diffusion into clinical practice, data provided by the NCQA suggests that rates of exposure have sustained small increases (approximately one percent increase for each condition) over the past three years (state of health care 2010). It is possible that increases are due to more attention to documenting conditions such as falls, but similar increases occurred for all three conditions including chronic kidney disease which is less commonly under-coded. This study does, however, provide a baseline to determine the extent to which diffusion of information included in this measure is reflected in VA clinical practice in the future, preferably in FY11 or FY12.

Finally, because falls are routinely under-coded it is likely that our estimates of Rx-DIs are conservative since only those with severe falls tend to be identified as such using administrative data.

This study found a relatively high rate of exposure to potentially harmful Rx-DIS for patients with dementia, falls and chronic renal failure, but generally lower rates than were found in Medicare data during the same time period.[16] However, studies to date have not examined the link between exposure and adverse outcomes using this less comprehensive HEDIS measure of Rx-DIS. Our study suggests that research examining outcomes should examine outcomes and risk factors for individual conditions separately before combining them as a single measure of exposure. If links between Rx-DIS are demonstrated, the VA is uniquely positioned to use health information technology to potentially reduce Rx-DIS exposure by implementing prescribing alerts within the electronic medication order process. As a leader in geriatric care, the VA is also in a position to test interventions such as use of

pharmacists or geriatricians within the Patient Aligned Care Teams (patient centered medical home) to improve the quality of care for older veterans, and to conduct investigations on how shared decision-making between patient and provider may contribute to, or be used to reduce, Rx-DIS exposure.

Acknowledgments

This study was supported by a VA Health Services Research grant (IIR-06–062). Dr Hanlon is supported by National Institute of Aging grants (R01AG027017, P30AG024827, T32 AG021885, K07AG033174, R01AG034056), a National Institute of Mental Health grant (R34 MH082682), a National Institute of Nursing Research grant (R01NR010135), and an Agency for Healthcare Research and Quality grant (R01HS017695). Dr. Horton is a recipient of the Geriatric Academic Career Award KO1 HP00114-02. We acknowledge the contributions of Jeffrey Tabares and Ranjani Davalath in assisting with manuscript preparation.

Sponsor's Role: The research's sponsor had no role or influence in matters relating to research design, methods, subject recruitment, data collections, analysis and preparation of paper.

Reference List

1. Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. Arch Intern Med. 1997; 157:1531–1536. [PubMed: 9236554]
2. Fick DM, Cooper JW, Wade WE, et al. Updating the Beers Criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. Arch Intern Med. 2003; 163:2716–2724. [PubMed: 14662625]
3. Zhan C, Sangl J, Bierman AS, et al. Potentially inappropriate medication use in the community-dwelling elderly: findings from the 1996 Medical Expenditure Panel Survey. JAMA. 2001; 286:2823–2829. [PubMed: 11735757]
4. Goulding MR. Inappropriate medication prescribing for elderly ambulatory care patients. Arch Intern Med. 2004; 164:305–312. [PubMed: 14769626]
5. Pugh MJ, Fincke BG, Bierman A, et al. Potentially inappropriate prescribing in elderly veterans: are we using the wrong drug, wrong dose, or wrong duration? J Am Geriatr Soc. 2005; 53:1282–1289. [PubMed: 16078952]
6. McLeod PJ, Huang AR, Tamblyn RM, et al. Defining inappropriate practices in prescribing for elderly people: a national consensus panel. CMAJ. 1997; 156:385–391. [PubMed: 9033421]
7. Lindblad CI, Hanlon JT, Gross CR, et al. Clinically important drug-disease interactions and their prevalence in older adults. Clin Ther. 2006; 28:1133–1143. [PubMed: 16982290]
8. Curtis LH, Ostbye T, Sendersky V, et al. Inappropriate prescribing for elderly Americans in a large outpatient population. Arch Intern Med. 2004; 164:1621–1625. [PubMed: 15302631]
9. Simon SR, Chan KA, Soumerai SB, et al. Potentially inappropriate medication use by elderly persons in U.S. Health Maintenance Organizations, 2000–2001. J Am Geriatr Soc. 2005; 53:227–232. [PubMed: 15673345]
10. Zhan C, Correa-de-Araujo R, Bierman AS, et al. Suboptimal prescribing in elderly outpatients: potentially harmful drug-drug and drug-disease combinations. J Am Geriatr Soc. 2005; 53:262–267. [PubMed: 15673350]
11. Lindblad CI, Artz MB, Pieper CF, et al. Potential drug-disease interactions in frail, hospitalized elderly veterans. Ann Pharmacother. 2005; 39:412–417. [PubMed: 15687479]
12. Hastings SN, Sloane RJ, Goldberg KC, et al. The quality of pharmacotherapy in older veterans discharged from the emergency department or urgent care clinic. J Am Geriatr Soc. 2007; 55:1339–1348. [PubMed: 17767675]
13. Hastings SN, Schmader KE, Sloane RJ, et al. Quality of pharmacotherapy and outcomes for older veterans discharged from the emergency department. J Am Geriatr Soc. 2008; 56:875–880. [PubMed: 18341519]
14. Chrischilles EA, VanGilder R, Wright K, et al. Inappropriate medication use as a risk factor for self-reported adverse drug effects in older adults. J Am Geriatr Soc. 2009; 57:1000–1006. [PubMed: 19507293]

15. Lund BC, Carnahan RM, Egge JA, et al. Inappropriate prescribing predicts adverse drug events in older adults. Ann Pharmacother. 2010; 44:957–963. [PubMed: 20460558]
16. [Accessed August 6, 2010] The state of health care quality: value, variation and vulnerable populations 2009. National Committee for Quality Assurance (online). Available at http://www.ncqa.org/Portals/0/Newsroom/SOHC/SOHC_2009.pdf.
17. [Accessed February 4, 2011] HEDIS 2008 NDC Lists. National Committee on Quality Assurance (online). Available at http://www.ncqa.org/tabid/598/Default.aspx.
18. Borzecki AM, Wong AT, Hickey EC, et al. Identifying hypertension-related comorbidities from administrative data: what's the optimal approach? Am J Med Qual. 2004; 19:201–206. [PubMed: 15532912]
19. Selim AJ, Fincke G, Ren XS, et al. Comorbidity assessments based on patient report: results from the Veterans Health Study. J Ambulatory Care Manage. 2004; 27:281–295. [PubMed: 15287217]
20. Selim AJ, Berlowitz DR, Fincke G, et al. Risk-adjusted mortality rates as a potential outcome indicator for outpatient quality assessments. Med Care. 2002; 40:237–245. [PubMed: 11880796]
21. Schneeweiss S, Seeger JD, Maclure M, et al. Performance of comorbidity scores to control for confounding in epidemiologic studies using claims data. Am J Epidemiol. 2001; 154:854–864. [PubMed: 11682368]
22. Pugh MJ, Copeland LA, Zeber JE, et al. The impact of epilepsy on health status among younger and older adults. Epilepsia. 2005; 46:1820–1827. [PubMed: 16302863]
23. Pugh MJ, Rosen AK, Montez-Rath M, et al. Potentially inappropriate prescribing for the elderly: effects of geriatric care at the patient and health care system level. Med Care. 2008; 46:167–173. [PubMed: 18219245]
24. Hanlon JT, Fillenbaum GG, Schmader KE, et al. Inappropriate drug use among community dwelling elderly. Pharmacotherapy. 2000; 20:575–582. [PubMed: 10809345]
25. Pugh MJ, Hanlon JT, Zeber JE, et al. Assessing potentially inappropriate prescribing in the elderly Veterans Affairs population using the HEDIS 2006 quality measure. J Manag Care Pharm. 2006; 12:537–545. [PubMed: 16981799]
26. Lindblad, CI.; Hanlon, JT.; Gross, CR., et al. Drug-Disease Interactions and Health Outcomes in Frail Elderly Veterans. Poster presented at the Annual Meeting of the American Geriatrics Society; 2006.
27. Fick DM, Waller JL, Maclean JR, et al. Potentially inappropriate medication use in a Medicare managed care population with higher costs and utilization. J Manag Care Pharm. 2001; 7:407–413.
28. Hanlon JT, Schmader KE, Boult C, et al. Use of inappropriate prescription drugs by older people. J Am Geriatr Soc. 2002; 50:26–34. [PubMed: 12028243]
29. Carey IM, De Wilde S, Harris T, et al. What factors predict potentially inappropriate primary care prescribing in older people? Analysis of UK Primary Care Patient Record database. Drugs Aging. 2008; 25:693–706. [PubMed: 18665661]
30. Frayne SM, Halanych JH, Miller DR, et al. Disparities in diabetes care: impact of mental illness. Arch Intern Med. 2005; 165:2631–2638. [PubMed: 16344421]
31. Zeber JE, Grazier KL, Valenstein M, et al. Effect of a medication copayment increase in veterans with schizophrenia. Am J Manag Care. 2007; 13:335–346. [PubMed: 17567234]
32. Kressin NR, Petersen LA. Racial differences in the use of invasive cardiovascular procedures: review of the literature and prescription for future research. Ann Intern Med. 2001; 135:352–366. [PubMed: 11529699]
33. Kales HC, Blow FC, Bingham CR, et al. Race, psychiatric diagnosis, and mental health care utilization in older patients. Am J Geriatr Psychiatry. 2000; 8:301–309. [PubMed: 11069270]
34. Szaflarski M, Szaflarski JP, Privitera MD, et al. Racial/ethnic disparities in the treatment of epilepsy: what do we know? What do we need to know? Epilepsy Behav. 2006; 9:243–264. [PubMed: 16839821]
35. Bierman AS, Pugh MJ, Dhalla I, et al. Sex differences in inappropriate prescribing among elderly veterans. The American Journal of Geriatric Pharmacotherapy. 2007; 5:147–161. [PubMed: 17719517]

36. Schmader KE, Hanlon JT, Pieper CF, et al. Effects of geriatric evaluation and management on adverse drug reactions and suboptimal prescribing in the frail elderly. Am J Med. 2004; 116:394–401. [PubMed: 15006588]

37. [Accessed October 16, 1909] Resources on the Medicare Prescription Drug Benefit. Kaiser Family Foundation (online). Available at http://www.kff.org/medicare/rxdrugbenefit.cfm.

38. Ray WA, Griffin MR, Schaffner W, et al. Psychotropic drug use and the risk of hip fracture. N Engl J Med. 1987; 316:363–369. [PubMed: 2880292]

Table 1

Description of Drug-Disease Interactions Identified by the HEDIS Drug-disease Interaction Measure

Disease States (N with condition/ disease)	Drugs to Avoid	N (% With Condition)	% Exposure 2006 in NCQA Study using Medicare data[16]
Dementia (N=131,808)	Anticholinergics, tricyclic antidepressants	26,640 (20.2)	24.6
Fall or Hip Fracture (N=54,393)	Antipsychotics, tricyclic antidepressants, sleep agents	8,806 (16.2)	14.6
Chronic Renal Failure (N=154,278)	NSAIDS	13,165 (8.5)	9.5
Prevalence of 1 or more Rx-DIS overall (N=305,041)		46,481 (15.2%)	19.4

Examples of anticholinergics include diphenhydramine, dicyclomine, promethazine, cyclobenzaprine, chlorpheniramine, and oxybutynin.

Results from a National Committee on Quality Assurance (NCQA) study examining Drug-Disease Interaction exposure based on the HEDIS measure in 2006 using Medicare data.[16]

Table 2

Descriptive Statistics: HEDIS Drug Disease Interaction (Rx-DIS) Exposure by Condition

Variables	Overall Rx-DIS		Dementia Rx-DIS		Fall Rx-DIS		CRF Rx-DIS	
	No (N=258,560)	Yes (N=46,481)	No (N=105,158)	Yes (N=26,650)	No (N=45,587)	Yes (N=8,806)	No Rx-DIS (N=141,113)	Yes (N=13,165)
Demographic Characteristics								
Age [Mean (SD)]	79.5 (5.7)	78.5 (5.9)	79.5 (5.8)	78.5 (5.9)	78.7 (6.5)	77.7 (6.4)	77.5 (6.1)	76.3 (6.0)
Sex: Male	253,897 (98.2)	42,216 (97.3)	102,832 (97.9)	25,884 (97.1)	43,726 (95.9)	8,371 (95.1)	139,733 (99.0)	13,020 (98.9)
Race: White	176,514 (68.3)	33,017 (71.0)	70,803 (67.4)	18,907 (71.0)	34,574 (75.8)	6,890 (78.3)	94,682 (67.1)	8,802 (66.9)
African American	27,445 (10.6)	5,323 (11.4)	10,399 (9.9)	2,620 (9.8)	4,071 (8.9)	786 (8.9)	17,837 (12.6)	2,176 (16.5)
Hispanic	10,924 (4.2)	2,940 (6.3)	5,432 (5.2)	1,835 (6.9)	2,219 (4.9)	556 (6.3)	5147 (3.7)	722 (5.5)
Other	3,695 (1.4)	670 (1.4)	1,391 (1.3)	345 (1.3)	697 (1.5)	137 (1.6)	2,122 (1.5)	214 (1.6)
Missing	39,982 (15.5)	4,531 (9.8)	17,054 (16.2)	2,943 (11.0)	4,026 (8.8)	433 (4.9)	21,316 (15.1)	1,251 (9.5)
Marital Status: Married	89,680 (34.8)	17.362 (37.5)	69,535 (66.4)	17,427 (65.6)	25,324 (55.7)	4,762 (54.3)	92,087 (65.5)	7,999 (60.9)
Health Status Factors								
Unique Medications (Mean [SD])	8.1 (4.9)	11.6 (5.5)	8.1 (4.9)	11.6 (5.5)	10.3 (5.8)	13.3 (5.9)	9.8 (5.3)	11.6 (5.5)
Selim Physical (Mean [SD])	4.3 (2.4)	4.9 (2.5)	3.7 (2.3)	4.6 (2.5)	5.2 (2.6)	5.5 (2.7)	4.7 (2.4)	5.2 (2.4)
Selim Mental: 0	192,019 (74.3)	26,367 (56.7)	66,229 (63.0)	13,453 (50.4)	30,958 (67.9)	3,600 (40.9)	114,289 (81.0)	10,091 (76.6)
1	48,815 (18.9)	12,681 (27.3)	27,536 (26.2)	8,360 (31.4)	10,358 (22.7)	2,908 (33.0)	20,348 (14.4)	2,157 (16.4)
2 or more	17,726 (6.9)	7,433 (16.0)	11,314 (10.8)	4,837 (18.2)	4,271 (9.4)	2,294 (26.1)	6,467 (4.6)	917 (7.0)
Access to Care Factors								
Copay Status:[+]								
Exempt	182,941 (70.8)	37,567 (80.8)	75,418 (71.8)	21,334 (80.0)	36,812 (80.8)	7,747 (88.0)	98,629 (69.9)	10,411 (79.1)
Geriatric Care:								
Yes	16,401 (6.3)	3,519 (7.6)	11,434 (10.9)	2,337 (8.8)	4,131 (9.1)	1,061 (12.0)	5,757 (4.1)	412 (3.1)
Primary Care:								
0–1 Visits	42,860 (16.5)	4,813 (10.3)	21,597 (20.6)	3,088 (11.6)	4,797 (10.5)	712 (8.1)	20,217 (14.3)	1,134 (8.6)

J Am Geriatr Soc. Author manuscript; available in PMC 2012 July 06.

Variables	Overall Rx-DIS		Dementia Rx-DIS		Fall Rx-DIS		CRF Rx-DIS	
	No (N=258,560)	Yes (N=46,481)	No (N=105,158)	Yes (N=26,650)	No (N=45,587)	Yes (N=8,806)	No Rx-DIS (N=141,113)	Yes (N=13,165)
2–4 Visits	131,751 (51.0)	20,948 (45.1)	52,691 (50.1)	12,236 (45.9)	19,372 (42.5)	3,198 (36.3)	72,114 (51.1)	6,215 (47.2)
5+ Visits	83,949 (32.5)	20,720 (44.6)	30,791 (29.3)	11,326 (42.5)	21,418 (47.0)	4,892 (55.6)	48,773 (34.6)	5,816 (44.2)

[+].02% not classified

CRF: Chronic Renal Failure
Rx-DIS: Drug Disease Interaction

All comparisons significant ($p < .01$) except comparisons by marital status for dementia and falls Rx-DIS and gender for chronic renal failure Rx-DIS

Table 3

Predictors of Drug-Disease Interactions (RX-DIS) in Community Dwelling VA Patients by Condition/ Disease

Effect	Any Rx-DIS OR (95% CI)	Dementia Rx-DIS OR (95% CI)	Falls Rx-DIS OR (95% CI)	CRF Rx-DIS OR (95% CI)
Demographic Characteristics				
Age	1.0 (0.99–1.0)	0.98 (0.98–0.99)	.98 (.98–.99)	0.97 (0.97–0.98)
Race/ Ethnicity (vs. White)				
African American	0.98 (0.95–1.01)	0.88 (0.83–0.92)	1.03 (0.94–1.12)	1.17 (1.11–1.23)
Hispanic	1.25 (1.20–1.31)	1.07 (1.01–1.13)	1.19 (1.07–1.31)	1.35 (1.24–1.46)
Other	0.94 (0.89–1.03)	0.93 (0.82–1.06)	0.98 (0.81–1.19)	1.05 (0.91–1.21)
Women (vs Men)	1.40 (1.31–1.50)	1.43 (1.30–1.57)	1.12 (1.00–1.26)	1.08 (0.90–1.29)
Unmarried (vs. Married)	0.97 (0.95–0.99)	0.93 (0.90–0.96)	0.96 (0.92–1.01)	1.10 (1.05–1.14)
Health Status Factors				
Number of Unique Medications	1.09 (1.09–1.09)	1.13 (1.12–1.13)	1.09 (1.08–1.09)	1.04 (1.04–1.05)
Selim Physical	0.97 (0.97–0.98)	0.96 (0.96–0.97)	0.91 (0.90–0.92)	0.99 (0.98–1.00)
Selim Mental Health (vs. 0)				
1	1.63 (1.59–1.67)	1.17 (1.13–1.21)	2.08 (1.96–2.20)	1.01 (0.06–1.06)
2 or more	2.36 (1.28–2.43)	1.33 (1.27–1.39)	3.50 (3.28–3.74)	1.19 (1.10–1.28)
Access To Care Factors				
Not exempt from copay (vs Exempt)	0.78 (0.75–0.80)	0.85 (0.82–0.89)	0.75 (0.70–0.81)	0.76 (0.60–0.80)
Geriatric Care	1.01 (0.97–1.06)	0.68 (0.64–0.71	1.26 (1.16–1.36)	0.69 (0.62–0.77)
Primary Care Visits (vs. 0–1)				
2–4	1.12 (1.08–1.17)	1.28 (1.22–1.34)	0.94 (0.86–1.03)	1.38 (1.29–1.49)
5+	1.21 (1.16–1.26)	1.31 (1.24–1.38)	0.89 (0.80–0.98)	1.47 (1.36–1.59)

Rx-DIS: Drug Disease Interaction
CRF: Chronic Renal Failure
OR: Odds Ratio
CI: Confidence Interval