Published in final edited form as:

J Am Med Dir Assoc. 2017 September 01; 18(9): 806.e1–806.e17. doi:10.1016/j.jamda.2017.06.005.

Determinants of Potentially Inappropriate Medication Use in Long Term and Acute Care Settings: a Systematic Review

Stephanie K Nothelle, MD^a, Ritu Sharma, B.Sc^b, Allison H Oakes, BA^b, Madeline Jackson, BA^b, and Jodi B. Segal, MD, MPH^{a,b,c}

^aJohns Hopkins University School of Medicine, Department of Medicine, 1830 E Monument St, Baltimore, MD 21205

^bJohns Hopkins Bloomberg School of Public Health, 615 N Wolfe St, Baltimore, MD 21205

^cJohns Hopkins University Center for Health Services and Outcomes Research, Hampton House, 6th Fl, 624 N Broadway, Baltimore, MD 21205

Abstract

Background—Potentially inappropriate medications (PIM) are widely used in institutionalized older adults, yet the key determinants that drive their use are incompletely characterized.

Methods—We systematically searched published literature within MEDLINE® and Embase® from January 1998 to March 2017. We searched for studies conducted in the United States that described determinants of PIM use in adults ≥60 years of age in a nursing home or residential care facility, in the Emergency Department (ED), or in the hospital. Paired reviewers independently screened abstracts and full text articles, assessed quality and extracted data.

Results—Among 30 included articles, 12 examined PIM use in the nursing home or residential care settings, 4 in the ED, 12 in acute-care hospitals, and 2 across settings. The Beers criteria were most frequently used to identify PIM use, which ranged from 3.6 to 92%. Across all settings, the most common determinants of PIM use were medication burden and geographic region. In the nursing home, the most common additional determinants were younger age, and diagnoses of depression or diabetes. In both the ED and hospital, patients receiving care in the West, Midwest, and South, relative to the Northeast, were at greater risk of receiving a PIM. Very few studies examined clinician determinants of PIM use; geriatricians used fewer PIMs in the hospital than other clinicians.

Conclusions—Among older adults, those who are on many medications are at increased risk for PIM use across multiple settings. We propose that careful testing of interventions that target modifiable determinants are indicated to assess their impact on PIM use.

Corresponding author: Stephanie Nothelle, MD, 5200 Eastern Ave, MFL 7th Fl., Baltimore, MD 21224, 410-550-2805, 410-550-8701, snothell1@jhmi.edu.

Conflicts of Interest: None.

Funding source role: None.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Keywords

Overuse; inappropriate prescribing; long term care; acute care

INTRODUCTION

Clinicians have long recognized the risks from inappropriate use of medications in older adults. Of the ten recommendations from the American Geriatric Society to the Choosing Wisely initiative, six were about the use of medications in this patient population.¹ Despite this, inappropriate medication use remains prevalent.² Risky medication use is associated with falls³, adverse drug events⁴, hospitalization, and increased health care costs.⁵

However, inappropriate medication use is challenging to define. It is often referred to as *potentially* inappropriate medication (PIM) use, as there may be situations in which the use of the medication is appropriate. There are several published definitions for PIM,^{6–14} centered on these being medications where the risks from their use likely exceeds their benefits.⁶

Older adults residing in institutional settings such as nursing homes are at particularly high risk for PIM use.¹⁵ Hospitalization is also a setting in which older adults are likely to be exposed to PIMs.¹⁶ It remains unclear; however, what drives PIM use in these settings, which is central to the design of interventions to curb PIM use. Therefore, we sought to systematically review the literature to identify the determinants of PIM use in older adults in institutional settings: in nursing homes, emergency departments (EDs), and hospitals.

METHODS

Data Sources and Searches

We registered the protocol for this systematic review in Prospero (#42015029482). We searched MEDLINE® and Embase® from January 1998 through March 2017 using terms reflecting medical subject heading (MeSH) terms and key words relevant to the overuse of healthcare services. The literature addressing this key question about PIM use was identified among the results generated by the broader search for literature about overuse of health care services. We then updated the search from January 1998 through March 2017 for articles specifically addressing PIM use in nursing homes, EDs, and hospitals. The following search terms were used:

First search

“medical overuse” OR “health services misuse” OR health services overutilization OR “unnecessary procedures” OR medically unnecessary procedures OR Diagnostic Tests, Routine/utilization OR Defensive Medicine OR Practice Patterns OR Health Services Abuse OR Health Services Overuse OR medical overutilization OR inappropriate utilization

Second focused search

Overmedication OR “Potentially Inappropriate Medication List” “inappropriate prescribing” OR “polypharmacy” OR “inappropriate medication” OR “prescribing patterns” OR Prescription Drug Misuse OR Prescription Drug Overuse

Searches were limited to human studies in the English language for relevancy. We hand searched the reference lists of each included article as well as related systematic reviews for additional articles. The results of the searches were downloaded and imported into EndNote™ (New York, NY), duplicates were screened out, and the remaining articles were uploaded to DistillerSR (Evidence Partners, Ottawa, Ontario, Canada), a Web-based software package developed for systematic review data management. This database was used to track the search results at the levels of title review, abstract review, and article inclusion/exclusion.

Study Selection

Four authors (SN, RS, AO, MJ) participated in the review process, including two medical students (see acknowledgements). Two reviewers independently screened titles, abstracts, and the full-text in parallel and came to agreement on appropriateness for inclusion. Studies were included if they tested determinants of use of medications considered inappropriate or potentially inappropriate based on defined criteria (i.e., Beer’s list). We included studies examining patients older than age 60, written in English and that did not exclusively describe care outside of the United States. We further restricted the study to data collected after 1996, given the substantial changes in the U.S. healthcare system in the past two decades. We did not include studies testing interventions targeting medication use, except for a single study, which was a pragmatic trial of different existing care settings.¹⁷ Titles were included if at least one reviewer marked it for inclusion while it was excluded only if two reviewers agreed it was ineligible. At the abstract level, both reviewers had to indicate that an article was ineligible for it to be removed (Appendix Figure A1). Articles promoted on the basis of abstract review underwent another independent parallel review to determine if they should be included for data extraction (Appendix Figure A1). Differences between reviewers were resolved through consensus adjudication.

Data Extraction, Quality, and Applicability Assessment

Four authors (SN, RS, AO, MJ) participated in the abstraction and quality evaluation process, including one medical student (see acknowledgements). We created and piloted data extraction forms in Excel (Microsoft®, Redmond, WA). Reviewers extracted information on the study characteristics, study participant characteristics, methods of data collection, criteria used to define PIM, the determinants evaluated by the investigators and the determinants identified as being significantly associated with the overuse event. The determinants were classified as related to the patient, the clinician, or the environment including the region and health system. We used the criteria for determining statistical significance as had been defined by each article. One article reported only descriptive statistics which we used to calculate unadjusted odds ratios.¹⁸ One reviewer completed data abstraction and a second reviewer checked the first reviewer’s abstraction for completeness and accuracy. We resolved differences between reviewer pairs by discussion and, as needed, through full-team meetings.

Using the same parallel independent process, two reviewers assessed risk of bias in included articles using an adaptation of an assessment tool for cohort studies and an adaptation of a survey appraisal instrument.¹⁹ Differences between reviewers were resolved through consensus

Data Synthesis and Analysis

Four authors (SN, RS, AO, MJ) created detailed evidence tables and synthesized the results by setting and type determinants studied to create summary tables of the results (Appendix Table A1). The results were not amenable to quantitative pooling given the heterogeneity in design across studies.

Role of the Funding Source

The funding source had no role in this project.

RESULTS

We identified 12,500 titles meeting our criteria. (Appendix Figure A1) From these, we selected 730 articles for full-text review, of which 30 met our final criteria.

Risk of Bias

The risk of bias was determined to be low for 25 of the 30 studies; four were determined to have a moderate risk of bias.^{18,20–22} Only one study was considered to have a high risk of bias.²³ The primary source of bias was potential confounding due to inadequate adjustment of effect estimates. One cohort study did not clearly describe the characteristics of the study participants at enrollment.²⁴

Determinants of PIM Use in Nursing Homes and Residential Care—Twelve studies evaluated determinants of potentially inappropriate medication use by residents of nursing homes or residential care facilities (i.e. assisted living facilities).^{20,24–34}

Additionally, two studies of Medicaid claims examined populations of older adults that included a subgroup in the nursing home.^{29,35} Three of the studies limited their analyses to nursing home residents with dementia.^{25,31,32} All used multivariable analysis adjusting for some combination of patient and system level factors, except one.¹⁸ Individuals were demographically similar across studies and nine of the eleven studies used a version of the Beers list to define PIM (Table 1). Frequently examined determinants of PIM use are summarized in Table 2.

Patient Factors: Twelve studies evaluated patient factors contributing to PIM use in this setting (Appendix Table A1).^{20,24–34} The four largest studies reported that younger age was significantly associated with PIM use overall^{24,25} or specifically with inappropriate benzodiazepine or antipsychotic use.^{33,34} In two of three studies^{25,31,32} of residents with advanced dementia, men were more likely than women to have PIM use.^{25,32} In populations with mixed cognitive abilities, women were more likely than men to have used a PIM^{24,29} or a benzodiazepine,³³ but no association was observed between sex and antipsychotic use.³⁴ Three of the nine studies^{20,25,27,29–34} investigating race found racial determinants of PIM

use, but the directions differed by the studied population.^{25,31,33} Marital status,^{26,33} poverty,²⁶ education,^{26,30,31,34} and length of stay^{26,28,33} were not significant determinants of PIM use.

Twelve studies examined clinical factors.^{20,24–34} Seven studies exploring the association between medication count and PIM use found that residents on more medications were more likely to receive a PIM.^{20,26,28–31,34} Although in one survey this was significant only among those with advanced dementia, not those with mild to moderate dementia.³¹ Lesser cognitive impairment among nursing home residents without dementia was predictive of PIM use in three^{20,24,28} of the four studies³⁰ that investigated this. Mental health diagnoses increased risk of PIM use in four^{25,26,31,33} of five studies.³⁴ Other individual comorbidities were not consistently significant across studies with the exception of diabetes, which was positively associated with PIM use in three^{24,25,32} of the four studies investigating this.²⁸

Eight studies examined the residents' functional status and PIM use.^{20,24–26,30,32–34} Less impairment in activities of daily living was associated with PIM use in three.^{25,26,32} Among residents with severe dementia, severe medical illness as indicated by hospitalization in the last 90 days or a recent physician visit were associated with more PIM use.²⁵ The absence of a “Do Not Hospitalize” order was also associated with more PIM use in those with advanced dementia.^{25,32}

Clinician factors: No studies examined clinician factors associated with PIM use in nursing home or residential care residents.

System/Environmental factors: Thirteen studies evaluated system-level factors contributing to PIM use in a nursing home or residential care setting (Appendix Table A1).^{18,20,24–27,29–35} Five studies^{25,26,31,33,34} evaluated the relationship between census region and PIM use, with three finding statistically significant differences across regions.^{25,31,33} One study of Medicaid recipients in Kentucky found that those living in a nursing home were more likely to receive a PIM than those community-dwellers.³⁵ Larger nursing homes had more PIM use in one national survey,²⁶ while a multi-site study of residential care and assisted living facilities reported that smaller facilities had more PIM use.²⁰ Other studies of facility size were also inconsistent in their results.^{25,31,33,34} Although three surveys examined staffing as a predictor of PIM use,^{20,26,33} a low nurse to resident ratio (<1:20) was associated with more PIM use only in one large nation-wide survey.²⁶ Higher rather than low turnover of staff, having a low monthly cost to residents, and absence of a weekly clinician visit were all associated with more PIM use in residential care facilities.²⁰

Determinants of PIM Use in Older Patients in the Emergency Department—

Four studies evaluated determinants of PIM use in the ED.^{36–39} Participant demographics and percent of participants who received a PIM varied markedly (Table 1). All four studies used a version of the Beers criteria to define PIM (Table 1). All four studies used multivariate analyses adjusting for patient factors including age, sex, severity of illness on presentation and number of medications; three additionally adjusted for system-level factors.^{36,37,39} Frequently examined determinants of PIM use are summarized in Table 3.

Patient Characteristics: All four examined patient factors as determinants.^{36–39} Two surveys using National Hospital Ambulatory Medical Care Survey (NHAMCS) data found that younger persons and women were at higher risk of receiving a PIM^{36,37} with one reporting a significant interaction between age and sex, putting younger women at even higher risk.³⁶ Three studies^{36–38} evaluated race, with patients of white race significantly more likely to receive a PIM than those of black race in one national survey.³⁷

The number of medications initiated in the ED was a significant determinant of PIM use in the three largest studies.^{36–38} The two studies that examined urgency of the visit reported that those who presented with non-urgent rather than urgent concerns were more likely to have PIM use.^{36,37} In one study, discharged patients were more likely to receive a PIM than those admitted.³⁷

Clinician Characteristics: A single nationwide survey evaluated the association between clinician status (i.e. attending physician, midlevel provider, resident) and PIM use and found no association (Table 3, Appendix Table A1).³⁶

System/Environmental Characteristics: Two national surveys using NHAMCS data and one cohort study evaluated system-level factors (Appendix Table A1).^{36,37,39} The studies of NHAMCS data looked at regional variation and found that in comparison to the Northeast; the West, South and Midwest had more PIM use.^{36,37} These two national surveys also examined health insurance type and found no association with PIM use. The study which looked at NHAMCS data from 2000–2006, limited to discharged patients, found that EDs in rural settings or affiliated with for-profit hospitals had more PIM use than those in metropolitan settings or in public or non-profit hospitals.³⁶ While the study using earlier NHAMCS data, 1992–2000, found no relationship with rural or urban location and found that non-profit hospitals relative to public hospitals had more PIM use.³⁷ The cohort study examined time and day of the ED visit at a Veterans Affairs (VA) medical center and reported no significant association with PIM use.³⁹

Determinants of PIM Use in Hospitalized Patients—Twelve studies evaluated determinants of PIM use in the hospital at varying times during the admission.^{17,21–23,40–47} Three of the studies used data from the same randomized controlled trial of VA inpatients,^{44,46,47} but differed in their criteria to determine PIM use. Seven of the twelve studies used a version of the Beers criteria to define PIM. (Table 1) Study size varied from 31 participants to nearly 50,000. Participant demographics were similar across studies (Table 1). Frequently examined determinants of PIM use are summarized in Table 3.

Patient Factors: Seven studies evaluated patient factors^{22,40,42–44,46,47} with all but one²² evaluating age, sex and race (Appendix Table A1). In the two studies that analyzed national hospital data, the risk of receiving a PIM while hospitalized was higher for women^{40,43} and younger older adults;^{40,43} older age was significant in frail VA inpatients.⁴⁷ Race and marital status were inconsistent determinants of PIM use. Three studies reported that education^{44,46,47} and employment status^{44,46} were not significant determinants of PIM use.

Four^{42,44,46,47} of the seven studies examined number of medications as a determinant of PIM use and found that patients on more medications had more PIM use.^{42,45,47,49} One cross-sectional study found that having multiple prescribers was also associated with increased risk of PIM use.⁴⁶ Four studies^{42,44,46,47} examined a composite measure of comorbidity; two of these, evaluating a random sample of the same population of frail VA inpatients, found that comorbidity burden was significantly associated with PIM use.^{44,47}

Anemia, congestive heart failure, chronic lung disease, hypothyroidism were associated with PIM use in the two studies^{40,43} that examined these using national hospital data; however, anemia was not a significant predictor among VA inpatients at discharge.⁴⁶ Four studies^{43,44,46,47} examined depression and PIM use, with only one finding a significant association.⁴³ No study evaluated the impact of cognitive impairment.

Fair or poor self-rated health in comparison to excellent health was significantly associated with PIM use in one VA study.⁴⁴ Functional status was not significant in three studies.^{44,46,47} Length of stay was an inconsistent determinant in the two studies that examined this.^{22,42}

Clinician Factors: Eight studies evaluated whether clinician specialty contributed to PIM use in the inpatient setting (Appendix Table A1).^{17,23,40,42–46} Admitting service was not a significant risk factor, but discharge by a surgeon in comparison to an internist was associated with PIM use in one study.⁴² Three studies examined whether the presence of a geriatrician⁴³ or admission to a geriatrician-staffed unit^{17,45} was associated with PIM use. Geriatricians, in comparison to other medical specialists, were less likely to prescribe a PIM⁴³ and the presence of a geriatrician in the hospital was associated with a decreased likelihood of PIM use across that hospital.⁴³ Admission to a geriatric unit in comparison to a general medical ward was associated with a greater decrease in number of PIMs from admission to discharge in one study,⁴⁵ but overall PIM use on discharge was the same in geriatric units and the general medicine wards.^{17,45} One survey of physicians reported that barriers to appropriate inpatient prescribing are that the patient is taking too many medications, concerns about the cost of an alternative (presumably more appropriate) medication for the patient, patient requests for specific medications, and lack of access to pharmacists.²³

System/Environmental Factors: Eight studies evaluated system or environmental factors contributing to PIM use in the hospital (Appendix Table A1).^{17,21,22,40,41,43,45,46} Two studies, using bivariate analysis only, examined whether hospital admission or discharge was associated with significant changes in PIM use.^{21,41} The study of a convenience sample of hospitalized older adults, found that admission was a high risk time for PIM use,²¹ while the other study, examining Medicare claims from older adults with acute myocardial infarction found that discharge, but not admission, was associated with a significant increase in PIM use.⁴¹ Three of the eight studies evaluating geographical variation in PIM use found significant differences by region.^{40,41,43}

DISCUSSION

We identified a body of literature examining drivers of PIM use in older people; most (20 of 29 studies) used the Beers criteria to identify PIMs. Determinants did not appear to differ importantly according to the criteria used for classifying PIMs, except when criteria were restricted to a subclass of medications, such as psychotropics. In the nursing home, the most common determinants were younger age, and diagnoses of depression or diabetes. Cognitive ability and mental illness were also significant determinants of PIM use in nursing homes; while functional status, comorbidity burden, and insurance type were frequently examined but were inconsistently significant. Very few studies examined clinician determinants of PIM use, although specialty of the clinician was associated with PIM use in the hospital, favoring care delivered by geriatricians. Although few demographic factors were consistent *across* studies and settings, younger older people and women were commonly identified as at risk for PIM use. Women tend to use health services more than men⁴⁸ and thus may have more chances to receive a PIM. As some studies have described, as overall utilization of health care services increases, so does receipt of inappropriate care.⁴⁹

In both the ED and hospital, patients receiving care in the West, Midwest, and South, relative to the Northeast, were at greater risk of receiving a PIM. Geographic variation in overuse of health services has been reported in a number of different settings^{49–51} and has been hypothesized to be due to high specialist to primary care ratio,⁵⁰ malpractice pressure,⁵² differences in provider practice styles, socioeconomic status and regional health seeking behavior.⁵³ Thus, geographic differences in PIM use may be unsurprising.

Across settings, the most consistent determinant of PIM use was number of medications. This was also perceived by physicians to be the most prevalent barrier to appropriate prescribing.²³ The literature supports that with an increased number of medications comes an increased likelihood that at least one of the medications will be inappropriate. A longer medication list may be a marker of medical complexity, where medication regimens may appropriately conflict with guidelines and safe-use recommendations.⁵⁴ Miller et al found that for each medication added to an older adult's medication list, the risk of receipt of a PIM goes up 5.2%.⁵⁵ This relationship between the count of medications and the use of PIMs is almost certainly confounded by the number and types of comorbid illnesses that the patient has and by the frequency of interaction with the healthcare system. Some have inferred [insert Miller reference #54] that medication intensity is on the causal pathway, or is the mediator, from multimorbidity to the use of inappropriate medications, and that there are also pathways from quality enabling factors and complexity factors that lead to PIM use, independent of medication intensity. From our review of the literature, however, we know that this remains unanswered.

Several of the other identified determinants such as age, sex, and geographic region are not inherently modifiable but could be targeted through other interventions. Computerized decision supports, such as alerts when a clinician prescribes a PIM, or involvement of a multidisciplinary team including pharmacists and/or geriatricians has the potential to reduce inappropriate medication use.⁵⁶ Systematic reviews describing these interventions,^{56,57} including a Cochrane review about interventions in nursing homes,⁵⁷ report few positive

studies; further data from high quality studies is still needed to identify the impact of such interventions on patient outcomes.

To our knowledge, there are no other systematic reviews of determinants of PIM use in institutionalized older adults. One systematic review of international literature evaluated studies of inappropriate medication use as measured in insurance and social security databases among community-dwelling elderly.⁵⁸ This study included 19 articles from 5 countries including the United States. Thirteen articles assessed determinants of PIM use and reported, consistent with our findings, that female sex and a higher number of medications are associated with PIM use. The direction of the association of age with PIM use varied. Other systematic reviews have reported the effect of PIM use on health care utilization and cost,⁵ examined the rates of PIM use or the most commonly prescribed PIMs in the primary care setting⁵⁹ and at the end of life,⁶⁰ however, these reviews did not address the determinants of PIM use.

Our review has some limitations. First, as a systematic review on *potentially* inappropriate medication use, we cannot state that we have identified the determinants of *actual* inappropriate medication use. The tools used in the included studies to identify PIM use cannot account for use in patients for whom these medicines are appropriate, but this is a limitation of the tools. While most used the Beers criteria, studies made modifications to the list and others restricted the definition to specific subclasses such as anticholinergics or psychotropics. We chose to include articles with varying criteria for PIM, as there did not appear to be significant differences in determinants identified by PIM criteria. Our review therefore identifies determinants of use of medications that are generally considered inappropriate in older patients. Our findings of increased PIM use in younger older adults may reflect appropriate prescribing of these medicines in a population that may benefit. However, while PIM use in these patients may carry little risk at the time of initiation, the medication is likely to be continued as the patient ages and may become increasingly inappropriate over time.

Although articles targeting PIM use were likely to be identified with our search strategy, we may have missed those that looked at inappropriate use of a specific medication in older adults. Our findings may or may not be transferrable to other countries, as we limited our search strategy to articles on US populations given the different regulatory environment.

This review identifies many patient and system characteristics associated with PIM use, but few can be easily intervened upon and many were not consistently significant. Although criteria such as Beer's list are easily applied to large databases, the complexity of decision making for an individual patient is not captured. Future studies in this area may need to consider alternative methodologies, with application of more rigorous methods for causal inference, to discern the drivers of inappropriate prescribing.

Conclusion

This review demonstrates that patient and system-level determinants of PIM use vary across institutional settings. Younger age, female sex, polypharmacy, and geographic region are most consistently associated with PIM use. More research is needed regarding clinician level

determinants of PIM use and the relationship between medication count and PIM to more fully understand the observed prescribing patterns and opportunities for improvement.

Acknowledgments

This work was supported by the National Institute on Aging K24 [AG049036-01A1]; the Health Resource and Services Administration Geriatrics Workforce Enhancement Program [U1QHP28710]; the Agency for Healthcare Research and Quality [T32HS000029].

We would like to acknowledge Jean Pannikottu, BS and Monica Tung, BA who assisted with a portion of article screening (JP and MT) and data abstraction checking (MT).

References

1. Choosing Wisely. <http://www.choosingwisely.org/>
2. O'Connor MN, Gallagher P, O'Mahony D. Inappropriate prescribing: criteria, detection and prevention. *Drugs & aging*. Jun 01; 2012 29(6):437–452. [PubMed: 22642779]
3. Freeland KN, Thompson AN, Zhao Y, Leal JE, Mauldin PD, Moran WP. Medication use and associated risk of falling in a geriatric outpatient population. *The Annals of pharmacotherapy*. Sep; 2012 46(9):1188–1192. [PubMed: 22872750]
4. Chang CM, Liu PY, Yang YH, Yang YC, Wu CF, Lu FH. Use of the Beers criteria to predict adverse drug reactions among first-visit elderly outpatients. *Pharmacotherapy*. Jun; 2005 25(6):831–838. [PubMed: 15927902]
5. Hyttinen V, Jyrkka J, Valtonen H. A Systematic Review of the Impact of Potentially Inappropriate Medication on Health Care Utilization and Costs Among Older Adults. *Medical care*. Oct; 2016 54(10):950–964. [PubMed: 27367864]
6. Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. An update. *Archives of internal medicine*. Jul 28; 1997 157(14):1531–1536. [PubMed: 9236554]
7. Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults: Results of a US Consensus Panel of Experts. *Archives of internal medicine*. 2003; 163(22):2716–2724. [PubMed: 14662625]
8. Hanlon JT, Schmader KE, Samsa GP, et al. A method for assessing drug therapy appropriateness. *Journal of clinical epidemiology*. Oct; 1992 45(10):1045–1051. [PubMed: 1474400]
9. Holmes HM, Sachs GA, Shega JW, Hougham GW, Cox Hayley D, Dale W. Integrating palliative medicine into the care of persons with advanced dementia: Identifying appropriate medication use. *Journal of the American Geriatrics Society*. 2008; 56(7):1306–1311. [PubMed: 18482301]
10. McLeod PJ, Huang AR, Tamblyn RM, Gayton DC. Defining inappropriate practices in prescribing for elderly people: a national consensus panel. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne*. Feb 01; 1997 156(3):385–391.
11. 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. *Journal of the American Medical Association*. 2001; 286(22):2823–2829. [PubMed: 11735757]
12. American Geriatrics Society Beers Criteria Update Expert P. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society*. Apr; 2012 60(4):616–631. [PubMed: 22376048]
13. U.S. Centers for Medicare and Medicaid Services. [Assessed November 17, 2016] State Operations Manual, Appendix pp— Guidance to Surveyors for Long Term Care Facilities. Available at: http://cms.hhs.gov/manuals/Downloads/som107ap_pp_guidelines_ltcf.pdf
14. Healthcare Effectiveness Data and Information Set (HEDIS) Measures. <http://www.ncqa.org/hedis-quality-measurement/hedis-measures>
15. Gurwitz JH, Field TS, Judge J, et al. The incidence of adverse drug events in two large academic long-term care facilities. *The American journal of medicine*. Mar; 2005 118(3):251–258. [PubMed: 15745723]

16. Sinvani LD, Beizer J, Akerman M, et al. Medication reconciliation in continuum of care transitions: a moving target. *Journal of the American Medical Directors Association*. Sep; 2013 14(9):668–672. [PubMed: 23608529]
17. 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*. Mar; 2004 116(6):394–401. [PubMed: 15006588]
18. Stevenson DG, Dusetzina SB, O'Malley AJ, et al. High-risk medication use by nursing home residents before and after hospitalization. *Medical care*. 2014; 52(10):884–890. [PubMed: 25185637]
19. Critical Appraisal of a Survey. <https://www.cebma.org/wp-content/uploads/Critical-AppraisalQuestions-for-a-Survey.pdf>
20. Sloane PD, Zimmerman S, Brown LC, Ives TJ, Walsh JF. Inappropriate medication prescribing in residential care/assisted living facilities. *J Am Geriatr Soc*. 2002; 50(6):1001–1011. [PubMed: 12110058]
21. Hale LDS, Griffin AE, Cartwright OM, Moulin J, Alford SJ, Fleming RM. Potentially inappropriate medication use in hospitalized older adults: A DUE using the full Beers criteria. *Formulary*. 2008; 43(9):326–339.
22. Bonk ME, Krown H, Matuszewski K, Oinonen M. Potentially inappropriate medications in hospitalized senior patients. *American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists*. Jun 15; 2006 63(12):1161–1165. [PubMed: 16754742]
23. Ramaswamy R, Maio V, Diamond JJ, et al. Potentially inappropriate prescribing in elderly: Assessing doctor knowledge, confidence and barriers. *Journal of evaluation in clinical practice*. 2011; 17(6):1153–1159. [PubMed: 20630004]
24. Dosa D, Cai S, Gidmark S, Thomas K, Intrator O. Potentially inappropriate medication use in veterans residing in community living centers: Have we gotten better? *Journal of the American Geriatrics Society*. 2013; 61(11):1994–1999. [PubMed: 24219201]
25. Tjia J, Briesacher BA, Peterson D, Liu Q, Andrade SE, Mitchell SL. Use of medications of questionable benefit in advanced dementia. *JAMA Intern Med*. 2014; 174(11):1763–1771. [PubMed: 25201279]
26. Lau DT, Kasper JD, Potter DE, Lyles A. Potentially inappropriate medication prescriptions among elderly nursing home residents: their scope and associated resident and facility characteristics. *Health Serv Res*. 2004; 39(5):1257–1276. [PubMed: 15333108]
27. Covington LP, McCarrell J, Hoerster NS. Prevalence of anticholinergic medication use in the program of all-inclusive care for the elderly. *Consultant Pharmacist*. 2016; 31(3):168–174. [PubMed: 26975596]
28. Perri M III, Menon AM, Deshpande AD, et al. Adverse outcomes associated with inappropriate drug use in nursing homes. *Annals of Pharmacotherapy*. 2005; 39(3):405–411. [PubMed: 15671088]
29. Rigler SK, Perera S, Jachna C, Shireman TI, Eng M. Comparison of the association between disease burden and inappropriate medication use across three cohorts of older adults. *American Journal Geriatric Pharmacotherapy*. 2004; 2(4):239–247.
30. Gray SL, Hedrick SC, Rhinard EE, et al. Potentially inappropriate medication use in community residential care facilities. *Annals of Pharmacotherapy*. 2003; 37(7–8):988–993. [PubMed: 12841805]
31. Hanlon JT, Aspinall SL, Handler SM, et al. Potentially suboptimal prescribing for older veteran nursing home patients with dementia. *The Annals of pharmacotherapy*. Jan; 2015 49(1):20–28. [PubMed: 25380592]
32. Tjia J, Rothman MR, Kiely DK, et al. Daily medication use in nursing home residents with advanced dementia. *Journal of the American Geriatrics Society*. May; 2010 58(5):880–888. [PubMed: 20406320]
33. Stevenson DG, Decker SL, Dwyer LL, et al. Antipsychotic and benzodiazepine use among nursing home residents: findings from the 2004 National Nursing Home Survey. *The American journal of*

geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry. Dec; 2010 18(12):1078–1092. [PubMed: 20808119]

34. Gellad WF, Aspinall SL, Handler SM, et al. Use of antipsychotics among older residents in VA nursing homes. *Medical care*. Nov; 2012 50(11):954–960. [PubMed: 23047785]
35. Piecoro LT, Browning SR, Prince TS, Ranz TT, Scutchfield FD. A database analysis of potentially inappropriate drug use in an elderly medicaid population. *Pharmacotherapy*. Feb; 2000 20(2):221–228. [PubMed: 10678301]
36. Meurer WJ, Potti TA, Kerber KA, et al. Potentially inappropriate medication utilization in the emergency department visits by older adults: analysis from a nationally representative sample. *Acad Emerg Med*. 2010; 17(3):231–237.
37. Caterino JM, Emond JA, Camargo CA Jr. Inappropriate medication administration to the acutely ill elderly: A nationwide emergency department study, 1992–2000. *Journal of the American Geriatrics Society*. 2004; 52(11):1847–1855. [PubMed: 15507061]
38. Chin MH, Wang LC, Jin L, et al. Appropriateness of medication selection for older persons in an urban academic emergency department. *Academic Emergency Medicine*. 1999; 6(12):1232–1242. [PubMed: 10609925]
39. Hastings SN, Sloane RJ, Goldberg KC, Oddone EZ, Schmader KE. The quality of pharmacotherapy in older veterans discharged from the emergency department or urgent care clinic. *Journal of the American Geriatrics Society*. Sep; 2007 55(9):1339–1348. [PubMed: 17767675]
40. Finlayson E, Maselli J, Steinman MA, Rothberg MB, Lindenauer PK, Auerbach AD. Inappropriate medication use in older adults undergoing surgery: a national study. *J Am Geriatr Soc*. 2011; 59(11):2139–2144. [PubMed: 21883113]
41. Lund BC, Schroeder MC, Middendorff G, Brooks JM. Effect of hospitalization on inappropriate prescribing in elderly medicare beneficiaries. *Journal of the American Geriatrics Society*. 2015; 63(4):699–707. [PubMed: 25855518]
42. Morandi A, Vasilevskis E, Pandharipande PP, et al. Inappropriate medication prescriptions in elderly adults surviving an intensive care unit hospitalization. *Journal of the American Geriatrics Society*. 2013; 61(7):1128–1134. [PubMed: 23855843]
43. Rothberg MB, Pekow PS, Liu F, et al. Potentially inappropriate medication use in hospitalized elders. *Journal of hospital medicine*. 2008; 3(2):91–102. [PubMed: 18438805]
44. Hanlon JT, Artz MB, Pieper CF, et al. Inappropriate Medication Use among Frail Elderly Inpatients. *Annals of Pharmacotherapy*. 2004; 38(1):9–14. [PubMed: 14742785]
45. Edwards RF, Harrison TM, Davis SM. Potentially Inappropriate Prescribing for Geriatric Inpatients: An Acute Care of the Elderly Unit Compared to a General Medicine Service. *Consultant Pharmacist*. 2003; 18(1):37–49. [PubMed: 16563052]
46. Hajjar ER, Hanlon JT, Sloane RJ, et al. Unnecessary drug use in frail older people at hospital discharge. *Journal of the American Geriatrics Society*. Sep; 2005 53(9):1518–1523. [PubMed: 16137281]
47. Lindblad CI, Artz MB, Pieper CF, et al. Potential drug-disease interactions in frail, hospitalized elderly veterans. *The Annals of pharmacotherapy*. Mar; 2005 39(3):412–417. [PubMed: 15687479]
48. Blackwell DL, Lucas JW, Clarke TC. Summary health statistics for U.S. adults: national health interview survey, 2012. *Vital and health statistics. Series 10, Data from the National Health Survey*. Feb.2014 (260):1–161.
49. Makarov DV, Desai R, Yu JB, et al. Appropriate and inappropriate imaging rates for prostate cancer go hand in hand by region, as if set by thermostat. *Health affairs (Project Hope)*. Apr; 2012 31(4):730–740. [PubMed: 22492890]
50. Fisher ES, Wennberg DE, Stukel TA, Gottlieb DJ, Lucas FL, Pinder EL. The implications of regional variations in Medicare spending. Part 1: the content, quality, and accessibility of care. *Annals of internal medicine*. Feb 18; 2003 138(4):273–287. [PubMed: 12585825]
51. Colla CH, Morden NE, Sequist TD, Schpero WL, Rosenthal MB. Choosing wisely: prevalence and correlates of low-value health care services in the United States. *Journal of general internal medicine*. Feb; 2015 30(2):221–228. [PubMed: 25373832]

52. Baicker K, Buckles KS, Chandra A. Geographic variation in the appropriate use of cesarean delivery. *Health affairs (Project Hope)*. Sep-Oct;2006 25(5):w355–367. [PubMed: 16895942]
53. Jones WS, Patel MR, Dai D, et al. Temporal trends and geographic variation of lower-extremity amputation in patients with peripheral artery disease: results from U.S. Medicare 2000–2008. *Journal of the American College of Cardiology*. Nov 20; 2012 60(21):2230–2236. [PubMed: 23103040]
54. Uhlig K, Leff B, Kent D, et al. A framework for crafting clinical practice guidelines that are relevant to the care and management of people with multimorbidity. *Journal of general internal medicine*. Apr; 2014 29(4):670–679. [PubMed: 24442332]
55. Miller GE, Sarpong EM, Davidoff AJ, Yang EY, Brandt NJ, Fick DM. Determinants of Potentially Inappropriate Medication Use among Community-Dwelling Older Adults. *Health services research*. Sep 29.2016
56. Spinewine A, Schmader KE, Barber N, et al. Appropriate prescribing in elderly people: how well can it be measured and optimised? *Lancet (London, England)*. Jul 14; 2007 370(9582):173–184.
57. Alldred DP, Kennedy MC, Hughes C, Chen TF, Miller P. Interventions to optimise prescribing for older people in care homes. *The Cochrane database of systematic reviews*. Feb 12.2016 2:CD009095. [PubMed: 26866421]
58. Guaraldo L, Cano FG, Damasceno GS, Rozenfeld S. Inappropriate medication use among the elderly: a systematic review of administrative databases. *BMC Geriatr*. Nov 30.2011 11:79. [PubMed: 22129458]
59. Opondo D, Eslami S, Visscher S, et al. Inappropriateness of medication prescriptions to elderly patients in the primary care setting: a systematic review. *PloS one*. 2012; 7(8):e43617. [PubMed: 22928004]
60. Todd A, Husband A, Andrew I, Pearson SA, Lindsey L, Holmes H. Inappropriate prescribing of preventative medication in patients with life-limiting illness: a systematic review. *BMJ supportive & palliative care*. Jan 05.2016

References

1. Piecoro LT, Browning SR, Prince TS, Ranz TT, Scutchfield FD. A database analysis of potentially inappropriate drug use in an elderly medicaid population. *Pharmacotherapy*. Feb; 2000 20(2):221–228. [PubMed: 10678301]
2. Sloane PD, Zimmerman S, Brown LC, Ives TJ, Walsh JF. Inappropriate medication prescribing in residential care/assisted living facilities. *J Am Geriatr Soc*. 2002; 50(6):1001–1011. [PubMed: 12110058]
3. Gray SL, Hedrick SC, Rhinard EE, et al. Potentially inappropriate medication use in community residential care facilities. *Annals of Pharmacotherapy*. 2003; 37(7–8):988–993. [PubMed: 12841805]
4. Lau DT, Kasper JD, Potter DE, Lyles A. Potentially inappropriate medication prescriptions among elderly nursing home residents: their scope and associated resident and facility characteristics. *Health Serv Res*. 2004; 39(5):1257–1276. [PubMed: 15333108]
5. Rigler SK, Perera S, Jachna C, Shireman TI, Eng M. Comparison of the association between disease burden and inappropriate medication use across three cohorts of older adults. *American Journal Geriatric Pharmacotherapy*. 2004; 2(4):239–247.
6. Perri M III, Menon AM, Deshpande AD, et al. Adverse outcomes associated with inappropriate drug use in nursing homes. *Annals of Pharmacotherapy*. 2005; 39(3):405–411. [PubMed: 15671088]
7. Tjia J, Rothman MR, Kiely DK, et al. Daily medication use in nursing home residents with advanced dementia. *Journal of the American Geriatrics Society*. May; 2010 58(5):880–888. [PubMed: 20406320]
8. Stevenson DG, Decker SL, Dwyer LL, et al. Antipsychotic and benzodiazepine use among nursing home residents: findings from the 2004 National Nursing Home Survey. *The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry*. Dec; 2010 18(12):1078–1092. [PubMed: 20808119]

9. Gellad WF, Aspinall SL, Handler SM, et al. Use of antipsychotics among older residents in VA nursing homes. *Medical care*. Nov; 2012 50(11):954–960. [PubMed: 23047785]
10. Dosa D, Cai S, Gidmark S, Thomas K, Intrator O. Potentially inappropriate medication use in veterans residing in community living centers: Have we gotten better? *Journal of the American Geriatrics Society*. 2013; 61(11):1994–1999. [PubMed: 24219201]
11. Stevenson DG, Dusetzina SB, O'Malley AJ, et al. High-risk medication use by nursing home residents before and after hospitalization. *Medical care*. 2014; 52(10):884–890. [PubMed: 25185637]
12. Tjia J, Briesacher BA, Peterson D, Liu Q, Andrade SE, Mitchell SL. Use of medications of questionable benefit in advanced dementia. *JAMA Intern Med*. 2014; 174(11):1763–1771. [PubMed: 25201279]
13. Hanlon JT, Aspinall SL, Handler SM, et al. Potentially suboptimal prescribing for older veteran nursing home patients with dementia. *The Annals of pharmacotherapy*. Jan; 2015 49(1):20–28. [PubMed: 25380592]
14. Covington LP, McCarrell J, Hoerster NS. Prevalence of anticholinergic medication use in the program of all-inclusive care for the elderly. *Consultant Pharmacist*. 2016; 31(3):168–174. [PubMed: 26975596]
15. Caterino JM, Emond JA, Camargo CA Jr. Inappropriate medication administration to the acutely ill elderly: A nationwide emergency department study, 1992–2000. *Journal of the American Geriatrics Society*. 2004; 52(11):1847–1855. [PubMed: 15507061]
16. Meurer WJ, Potti TA, Kerber KA, et al. Potentially inappropriate medication utilization in the emergency department visits by older adults: analysis from a nationally representative sample. *Acad Emerg Med*. 2010; 17(3):231–237.
17. Chin MH, Wang LC, Jin L, et al. Appropriateness of medication selection for older persons in an urban academic emergency department. *Academic Emergency Medicine*. 1999; 6(12):1232–1242. [PubMed: 10609925]
18. Hastings SN, Sloane RJ, Goldberg KC, Oddone EZ, Schmader KE. The quality of pharmacotherapy in older veterans discharged from the emergency department or urgent care clinic. *Journal of the American Geriatrics Society*. Sep; 2007 55(9):1339–1348. [PubMed: 17767675]
19. Edwards RF, Harrison TM, Davis SM. Potentially Inappropriate Prescribing for Geriatric Inpatients: An Acute Care of the Elderly Unit Compared to a General Medicine Service. *Consultant Pharmacist*. 2003; 18(1):37–49. [PubMed: 16563052]
20. 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*. Mar; 2004 116(6):394–401. [PubMed: 15006588]
21. Hanlon JT, Artz MB, Pieper CF, et al. Inappropriate Medication Use among Frail Elderly Inpatients. *Annals of Pharmacotherapy*. 2004; 38(1):9–14. [PubMed: 14742785]
22. Lindblad CI, Artz MB, Pieper CF, et al. Potential drug-disease interactions in frail, hospitalized elderly veterans. *The Annals of pharmacotherapy*. Mar; 2005 39(3):412–417. [PubMed: 15687479]
23. Hajjar ER, Hanlon JT, Sloane RJ, et al. Unnecessary drug use in frail older people at hospital discharge. *Journal of the American Geriatrics Society*. Sep; 2005 53(9):1518–1523. [PubMed: 16137281]
24. Bonk ME, Krown H, Matuszewski K, Oinonen M. Potentially inappropriate medications in hospitalized senior patients. *American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists*. Jun 15; 2006 63(12):1161–1165. [PubMed: 16754742]
25. Rothberg MB, Pekow PS, Liu F, et al. Potentially inappropriate medication use in hospitalized elders. *Journal of hospital medicine*. 2008; 3(2):91–102. [PubMed: 18438805]
26. Hale LDS, Griffin AE, Cartwright OM, Moulin J, Alford SJ, Fleming RM. Potentially inappropriate medication use in hospitalized older adults: A DUE using the full Beers criteria. *Formulary*. 2008; 43(9):326–339.

27. Ramaswamy R, Maio V, Diamond JJ, et al. Potentially inappropriate prescribing in elderly: Assessing doctor knowledge, confidence and barriers. *Journal of evaluation in clinical practice*. 2011; 17(6):1153–1159. [PubMed: 20630004]
28. Finlayson E, Maselli J, Steinman MA, Rothberg MB, Lindenauer PK, Auerbach AD. Inappropriate medication use in older adults undergoing surgery: a national study. *J Am Geriatr Soc*. 2011; 59(11):2139–2144. [PubMed: 21883113]
29. Morandi A, Vasilevskis E, Pandharipande PP, et al. Inappropriate medication prescriptions in elderly adults surviving an intensive care unit hospitalization. *Journal of the American Geriatrics Society*. 2013; 61(7):1128–1134. [PubMed: 23855843]
30. Lund BC, Schroeder MC, Middendorff G, Brooks JM. Effect of hospitalization on inappropriate prescribing in elderly medicare beneficiaries. *Journal of the American Geriatrics Society*. 2015; 63(4):699–707. [PubMed: 25855518]

Appendix Figure 1.

Flow diagram of inclusion and exclusion process.

* Reviewers did not need to agree on reason for exclusion

Table 1

Summary Characteristics of Included Studies by Site of Care

Site of care (number of included studies)	Participant Demographics	PIM Criteria	Prevalence of PIM use
Nursing Home or Residential Care (n=14)	Age: <ul style="list-style-type: none"> Majority >85 years^{20,25,28,32} Majority >75 years^{18,24,26,27,30,31,33,29,34} NR³⁵ Sex: <ul style="list-style-type: none"> >70% women except VA studies which were 2% women^{24,31, 34} Race: <ul style="list-style-type: none"> >70% white except 2 studies without description of racial background^{26,28} 	<ul style="list-style-type: none"> Holmes^{25,32} Beers 1997^{20,26,28–30,35} Beers 2003, modified¹⁸ Beers 2012, anticholinergics²⁷ Beers 2012 and Holmes³¹ HEDIS 2006²⁴ Inappropriate antipsy³⁴ and benzo.³³ 	<ul style="list-style-type: none"> 16–54% of residents Antipsy and benzo. 9–15%³³ Antipsy 27% NR²⁷
Emergency Department (n=4)	Age: <ul style="list-style-type: none"> Mean age 74–77 years NR³⁷ Sex: <ul style="list-style-type: none"> Majority women^{36,38} 2% women³⁹ NR³⁷ Race: <ul style="list-style-type: none"> Majority African American³⁸ Majority white³⁶ NR^{37,39} 	<ul style="list-style-type: none"> Beers 1997 modified^{37,38} Beers 2003 modified^{36,39} 	<ul style="list-style-type: none"> 4–17% of visits
Inpatient Hospital (n=12)	Age: <ul style="list-style-type: none"> >50% >75 years^{17,21,40,41,43,45} >45% >75 years^{44,46,47} Mean age 68 years⁴² NR^{22,23} Sex: <ul style="list-style-type: none"> >45% women^{21,40–43,45} 2% women^{17,44,46,47} NR^{22,23} Race: <ul style="list-style-type: none"> >70% white^{17,40} 	<ul style="list-style-type: none"> Zahn⁴⁰ MAI^{17,44,46} HEDIS 2011⁴¹ Beers 1997⁴⁵ Beers 2003 modified^{22,42,43} Beers 2003^{21,23} Beers 1997 and McLeod⁴⁷ 	<ul style="list-style-type: none"> 9–92% of patients NR¹⁷ NA²³

Site of care (number of included studies)	Participant Demographics	PIM Criteria	Prevalence of PIM use
	• NR ^{21–23,45}		

NR = Not reported, NA = Not applicable (study of vignettes), VA= Veterans Affairs, MAI= Medication Appropriateness Index, HEDIS=Healthcare Effectiveness Data and Information Set, PIM = potentially inappropriate medication, Antipsy=antipsychotic medication, benzo= benzodiazepine

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 2
Frequently Examined Determinants of PIM Use Amongst Nursing Home and Care Facility Residents

Author, Year	Bivariate Only	Patient Factors				System Factors				
		Age	Sex	Race	Count of Medications	Physical Comorbidities	Psychiatric Comorbidities	Region	Rural vs. Urban	Insurance type
Survey										
Sloane, 2002 ²⁰		Ø	Ø	Ø	↑					
Gray, 2003 ³⁰		Ø	Ø	Ø	↑					
Lau, 2004 ²⁶		Ø	Ø		↑		★	Ø	Ø	★
Stevenson, 2010 ³³	Y	↓	F	★			★	★	Ø	★
Cross-sectional										
Piccoro, 2000 ³⁵ *										
Gellad, 2012 ³⁴		↓	Ø	Ø	↑		Ø	Ø	Ø	
Dosa, 2013 ²⁴		↓	F			★				
Tjia, 2014 ²⁵		↓	M	★		★	★	Ø		Ø
Covington, 2016 ²⁷		Ø	Ø	Ø		Ø				
Cohort										
Rigler, 2004 ²⁹		Ø	F	Ø	↑	Ø				
Perri, 2005 ²⁸		Ø	Ø		↑	Ø	Ø			
Tjia, 2010 ³²		Ø	M	Ø		★				
Stevenson, 2014 ¹⁸ †	Y									
Hanlon, 2015 ³¹		Ø	Ø	★	↑	Ø	★	★	★	

Blank cells indicate that the variable was not examined.

* Compared PIM use amongst nursing home residents to community dwelling older adults.

† Compared PIM use amongst nursing home residents before and 30 days following hospital admission.

↓ significant negative association, ↑ significant positive association, Ø = Not significant, ★ =significant, reference Supplementary Table S1 for specific result, F = female, M = male, Y = yes

Table 3
Frequently Examined Determinants of PIM Use in the Emergency Department and Hospital

Author, Year	Bivariate Only	Patient Factors					Clinician Factors		System Factors				
		Age	Sex	Race	Count of Medications	Physical Comorbidities	Psychiatric Comorbidities	Specialty/Type *	Geri Care	Region	Rural v. Urban	Insurance	
Emergency Department													
Cohort													
Chin, 1999 ³⁵		Ø	Ø	Ø	↑								
Hastings, 2007 ³⁶		Ø	Ø		Ø	Ø							
Survey													
Caterino, 2004 ³⁴		↓	F	★	↑					★	Ø	Ø	Ø
Meuer, 2010 ³³		↓	F	Ø	↑					★	Rural	Ø	Ø
Hospital													
Cohort													
Edwards, 2003 ⁴³	Y								★				
Rothberg, 2008 ⁴¹		↓	F						★	★	Ø		★
Hale, 2008 ⁴⁰ ‡	Y												
Finlayson, 2011 ³⁷		↓	F	★		★		★		★	Ø		
Morandi, 2013 ³⁹		Ø	Ø	Ø	↑	Ø		Ø		★			
Lund, 2015 ³⁸ ‡	Y									★			
Cross sectional													
Hanlon, 2004 ⁴²		Ø	Ø	Ø	↑			Ø					
Hajjar, 2005 ⁴⁴		Ø	Ø	Ø	↑	★		Ø					
Linblad, 2005 ⁴⁶	Y	↑	Ø	Ø	↑	Ø		Ø					
Bonk, 2006 ⁴⁵	Y												
RCT													
Schmader, 2004 ¹⁷									★				
Survey													

Author, Year	Bivariate Only	Patient Factors					Clinician Factors		System Factors			
		Age	Sex	Race	Count of Medications	Physical Comorbidities	Psychiatric Comorbidities	Specialty/Type [*]	Geri Care	Region	Rural v. Urban	Insurance
Ramaswamy, 2010 ²⁰ , §												

Blank cells indicate that the variable was not examined.

* Nurse practitioner v. Physician assistant v. Attending physician

‡ Compared PIM use per home medication list to PIMs given at admission and at discharge.

‡ Examined changes in PIM use associated with hospitalization in the long term (6 months pre- and post-) and in the short term (admission and discharge).

§ Survey of physician barriers to appropriate prescribing

↓ significant negative association, ↑ significant positive association, Ø = Not significant, ★=significant, reference Supplementary Table S1 for specific result, F= female, M= male, Y= yes
RCT=Randomized Controlled Trial

Appendix Table A1

Study Characteristics and Determinants of Potentially Inappropriate Medication (PIM) Use Examined in Included Articles.

Author, Year Study Design Data Source	Population n = Observations of PIM Events	Criteria for PIM	Patient Factors	Clinician factors	System/Environmental Factors
Nursing homes and Residential Care Facilities					
Picoro, 2000 ¹ Cross-sectional Retrospective Medicaid Pharmacy Claims	KY Medicaid recipients aged 65+ who filled a prescription 27% of elderly Medicaid recipients received a potentially inappropriate med	Beers 1997-except those dependent on dose, duration or over the counter	Age [65–84, ref: 85+], race [white, ref: black], sex [female], # of physicians [3– 5<6–10<10, ref: 1–2], # of prescriptions [increasing amounts, 37–60<61–120<120+, ref: 0–36]	None	Residence [nursing home, ref: community dwelling]
Sloane, 2002 ² Survey Collaborative Studies of Long-Term Care	Residents of 193 residential care/assisted living facilities in Florida, New Jersey, North Carolina, and Maryland n = 369 prescriptions (3.2%) to 322 residents (16%)	Beers 1997-except flecainide, phenylbutazone, cyclobenzaprine, haloperidol, thioridazine, non- sedating antihistamines, drugs dependent on dosage (iron and digoxin), short acting benzodiazepines, trazodone	Age, sex, race/ethnicity, dementia severity [no or mild dementia, Ref: moderate or severe dementia] , family or friend visits at least weekly, ADL dependency, # of medications [4–8 and >9 medications, Ref: <4 medications]	None	Number of beds [smaller], square of bed size, Medicaid status, for profit status, affiliation with nursing home, weekly doctor visit [did not have, Ref: weekly visits] , weekly nursing, moderate vs. high monthly rate [low minimum monthly rate, Ref: high minimum monthly rate] , RN/ resident ratio, LPN/resident ratio, nurse assistant/resident ratio, turnover of RN, turnover of LPN [Moderate LPN turnover, Ref: low LPN turnover] , turnover of PCA, facility type (small vs. traditional vs. new/ modern)
Gray, 2003 ³ Survey In-person interviews and state databases	Community Residential Care Facilities in a 3-county area in Washington State n = 62 (22%) residents took 75 PIMs	Beers 1997 included clonazepam, clorazepate, and prezeepam in the subclass of long-acting benzo, did NOT examine digoxin	Age, sex, race, high school education, fair/poor health (ref group unknown, significant at baseline only) , needs assistance with >=1 ADL, has cognitive impairment, # of prescription medications (significant at baseline only)	None	Adult family home, assisted living, adult residential care
Lau, 2004 ⁴ Survey Medical Expenditure Panel Survey Nursing Home Component	Nationally representative sample of nursing home residents in 1996 n = 50.3% of NH residents residing in a nursing home for 3 months or longer	Beers 1997	Age, sex, race, marital status, living children, education, poverty, # of days in NH, admitted before 1996, mental status (diagnosis of dementia, diagnosis of mental disorder, no mental disorder) [other, non-dementia mental disorder, ref: no mental disorder] # of ADL limitations [limitation in 4–5 ADLs, ref: 6 ADLs] , behavior problems (y/n), communication problems (y/n)	None	Census region, Metropolitan statistical area, county-level income [>25–30k per capita income in county, ref: >30K per capita income] , # of nursing home beds/200 or more beds, ref: 3–49 beds] , # of nursing home beds available, Medicaid status [Medicaid coverage, ref: no Medicaid coverage] , For profit status of NH, type of NH (hospital based, multiple levels of care), NH accreditation status [non-accredited facility, ref: accredited facility] .

Author, Year Study Design Data Source	Population n = Observations of PIM Events	Criteria for PIM	Patient Factors	Clinician factors	System/Environmental Factors
Rigler, 2004 ⁵ Retrospective cohort Claims	15% random sample of Kansas Medicaid beneficiaries >65 years n= 21% of 1163 ambulatory persons n= 48% of 858 frail persons n= 38% of 1164 nursing home residents	Beers 1997-excluding disease and dose dependent	[no communication problems, ref: communication problems], # of prescriptions drugs per month [5 or more drugs per month, ref: <5 drugs per month] <i>Stratified by ambulatory, frail and nursing home:</i> AMBULATORY: age, sex (female) [ref: male], # of medications per month (more), disease burden (CIRS- G) [2 or more], race FRAIL: age, sex (female) [ref: male], # of medications per month (more), disease burden (CIRS- G) [2-3 or 6+], race NURSING HOME: age, sex (female) [ref: male], # of medications per month (more), disease burden, race	None	certification status, RN to non-RN ratio, RN to resident ratio [<1:20, ref: >1:10], Pharmacist on site weekly, psychologist/psychiatrist on site weekly, technological services offered, % vaccinated for influenza
Perri, 2005 ⁶ Retrospective cohort- chart review	Medicaid NH residents in 15 Georgia facilities at high risk of polypharmacy, 2002 n=46.5% of 1117 patients	Beers 1997	Age, sex, LOS at NH, resuscitation status, # of medications (OTC and prescription) [higher], diagnosis of dementia [present, ref: absent], diagnosis of heart disease, diagnosis of HTN, diagnosis of arthritis, diagnosis of depression, diagnosis of fracture, diagnosis of stroke, diagnosis of diabetes, diagnosis of anemia, diagnosis of asthma, diagnosis of cancer	None	None
Tjia, 2010 ⁷ , Prospective Cohort Choices, Attitudes, and Strategies for Care in Advanced Dementia at the End- of-Life (CASCADE) study MDS, medical records, Mental status exam interviews with proxies, nurses	NH residents >65 years old with advanced dementia in the Boston area 2003-2006- n=329 persons, 37.5%	Holmes criteria	Age, sex [male], race, length of stay [shorter, ref: longer], cause of dementia, level of cognitive impairment, level of functional impairment (28 point ADL scale BANS-S scale) [lower score, more functional, ref: higher score, less functional], comorbidities (CV disease, DM, cancer) [DM present, ref: absent], acute illness in last 90 days, hospitalizations in the last 90 days, DNH order [DNH order present, ref: absent], feeding tube use, hospice	None	Special dementia care unit, NP or physician visit in the last 90 days

Author, Year Study Design Data Source	Population n = Observations of PIM Events	Criteria for PIM	Patient Factors	Clinician factors	System/Environmental Factors
Stevenson, 2010 ⁸ National Nursing Home Survey	Nationally representative survey of NH residents in 2004 n=9852 for whom benzo use may not be appropriate n= 8554 for whom antipsychotic prescribing may not be appropriate	"Resident diagnoses were considered in categorizing antipsychotic or benzo use as having an appropriate, potentially appropriate, or no appropriate indication. Categorizations were determined a priori based on Centers for Medicare Services survey protocols and interpretive guidelines."	referral, goal of care (comfort v. life prolongation) per proxy Antipsychotics: Sex, race, age [younger], marital status, behavioral symptoms [any symptoms, higher], ADL limitations, LOS, dementia [present, ref: absent], depression [present, ref: absent] Benzodiazepines: Sex [female], race [white, ref: non-white], age [younger], marital status, behavioral symptoms [any symptoms, higher], ADL limitations, LOS, dementia, depression	None	Antipsychotics: Chain nursing home, ownership, beds, RN FTE per resident, CNA FTE per resident, individual resident payer, share of patients with Medicaid as primary payer [higher share of Medicaid patients, ref: lower share], share of patients with Medicare as primary payer [lower share of Medicare patients, ref: higher share], census region [NE, ref: MW and W], metropolitan status [MSA, ref: non- MSA] Benzodiazepines: Chain nursing home [not a chain, ref: chain], ownership beds, RN FTE per resident, CNA FTE per resident, individual resident payer, share of patients with Medicaid as primary payer, share of patients with Medicare as primary payer, geographic region [S, ref: NE], MSA
Gellad, 2012 ⁹ Cross-sectional VA administrative database	VA NH residents >65 years from 2004–2005 n=3692	Centers for Medicare Services guidelines for appropriate use of antipsychotics	Age [<75, ref: 75+], race, sex, education, comorbidity index score [lower], ADL dependence, aggressive behavior [more], physical restraint use, diagnosis of Post Traumatic Stress Disorder, diagnosis of anxiety, diagnosis of depression, number of medications [more], antidepressant use [yes, ref: no], anxiolytic use [yes, ref: no], dementia treatment, residence in Alzheimer's unit [yes, ref: no]	None	Rural v. urban location, geographic region, facility size
Dosa, 2013 ¹⁰ Cross-sectional VA administrative database	VA NH residents >65 years from 2004–2009 n=28970 persons (16.4%)	HEDIS 2006	Age [<75, ref: 75+], sex [female], race, comorbid illness (CHF, DM, Stroke, Cancer, COPD, chronic renal failure) [COPD present, ref: absent] [DM present, ref: absent] [renal disease present, ref: absent] [cancer present, ref: absent], dementia [no to mild dementia, ref: moderate-	None	Facility fixed effects

Author, Year Study Design Data Source	Population n = Observations of PIM Events	Criteria for PIM	Patient Factors	Clinician factors	System/Environmental Factors
			severe dementia], function (ADL score 0–28)		
Stevenson, 2014 ¹¹ Retrospective cohort Medicare Beneficiary Summary, Medicare Provider and Analysis Review (MedPAR) inpatient claims, Omnicare pharmacy claims	Dual eligible NH residents >65 years who were hospitalized in 2008 n=21% of 52559 persons	Beers 2003-excluding disease dependent	None	None	Hospitalization [No PIM use prior to admission; PIM use increased on readmission, decreased 30 days following PIM use prior to admission; PIM use decreased on readmission, increased 30 days following]
Tjia, 2014 ¹² , Cross-sectional Prescription- dispensing database linked to MDS	Nationwide sample of NH residents >65 years with advanced dementia 2009–2010 n=2911 (53.9%) of residents	Holmes list: Published list created using Delphi process for patients with advanced dementia and palliative approach to care	Age [65–84, ref: >85], sex [male], race/ethnicity [Hispanic, ref: white; white, ref: black], ADL score [≤28, ref: score 28+], comorbid diabetes [DM present, ref: absent], comorbid heart failure, comorbid hypertension, comorbid stroke, comorbid osteoporosis, comorbid depression, nutritional problems, oral problems [absent, ref: present], feeding tube status, behavioral index score, DNR order [absent, ref: present], hospice enrollment [none, ref: hospice enrollment]	None	Special care unit residence [residence, ref: no residence], unit with >100 beds, facility % of residents with feeding tubes [highest or second highest tercile of feeding tube use, ref: lowest tercile of feeding tube use], facility % of residents antipsychotics prescribed, facility % of residents with DNR order, facility % of residents with advance directives, facility geographic region by census region [Pacific, West South Central or East South Central census region, ref: Mid-Atlantic], Medicaid status, physician visit in the last 14 days [present, ref: absent], hospitalization in the last 90 days [present, ref: absent]
Hanlon, 2015 ¹³ Retrospective cohort MDS, medication dispensing info, medical SAS files	Residents with dementia living in one of 133 VA NHs from 2004–2005 n=293 (27.2%) of residents with mild-moderate dementia n= 57 (25.1) of residents with severe dementia	Two criteria 1) Holmes criteria for those with severe dementia and 2) adaptation of Beers 2012 for those with mild-moderate dementia	Severe dementia: age, race, sex, education, comorbidity index, # of medications, bipolar, schizophrenia, memantine use, antidepressant use, antipsychotic use [present, ref: absent], hypnotic use Mild to moderate dementia: age, race [white, ref: black], sex, # education, comorbidity index, # of medications, bipolar, schizophrenia, memantine use, antidepressant use [present, ref: absent], antipsychotic use [present, ref: absent], hypnotic use	None	Severe dementia: bed size, rural v urban [rural, ref: urban], region Mild to moderate dementia: bed size, rural v urban, region [NE, ref: MW and S]
Covington, 2016 ¹⁴ Cross-sectional	Persons living in PACE and long-term facilities aged 65+ in 2013	Beers 2012 medications with strong anticholinergic properties	Age, race, sex, serum creatinine, creatinine clearance	None	PACE or long term care facility [long term care facility, ref: PACE]

Author, Year Study Design Data Source	Population n = Observations of PIM Events	Criteria for PIM	Patient Factors	Clinician factors	System/Environmental Factors
Medical charts and records	n=2.3% of 128 PACE participants n= 3.9% of 105 Long-term Care residents				
Emergency department					
Caterino, 2004 ¹⁵ Survey National Hospital Ambulatory Medical Care Survey	Nationally representative sample of patients >65 in EDs from 1992–2000 n= 12.6% of visits (population estimate 16,073,000)	Beers 1997 except dose, duration, condition dependent	Age [65–84 years, ref: 85+], sex [female], race/ethnicity, # of medications [2–6 medication, ref: 0–1], visit urgency [non-urgent visit, ref: urgent/emergent], admission status [discharged or other, ref: admitted]	None	Insurance type, HMO status, hospital ownership [voluntary, non-profit, ref: government owned], MSA, geographic region [MW, S or W, ref: NE]
Meuer, 2010 ¹⁶ Survey National Hospital Ambulatory Medical Care Survey	Nationally representative sample of patients >65 who were seen and discharged from the ED n= 5926 visits (population estimate 19,432,635)	Beers 2003 except medications inappropriate in certain doses, duration of administration or comorbid conditions were not included	Age [75+, ref: >75 years] sex [female], race/ethnicity, visit associated with injury [associated with an injury, ref: visit not associated with an injury], # of medications prescribed [2 or more medications, ref: 0–1 medications], urgency of issue [“non-urgent” issues triaged to be seen >1 hour, ref: urgent issues triaged to be seen immediately]	Attending status, resident status, midlevel status	MSA status (non-MSA locations, ref: MSA location hospital), geographic region [West, ref: Northeast], health insurance type, hospital ownership structure [for-profit hospital, ref: non-profit]; year of visit [earlier in study period]
Chin, 1999 ¹⁷ Prospective Cohort Chart review and interview	Patients >65 seen at the University of Chicago ED from 1995–1996 n=133 people (14.8%)	Beers 1997 excluding dose dependent	Age, sex, race, marital status, education, could use more help at home, functional status, # of medications on home list [higher], # of medications given in ED [higher], # of diseases, functional status, HRQoL scores, # of prior admissions in the last 6 months, requiring a proxy for responses	None	None
Hastings, 2007 ¹⁸ Retrospective cohort Medical records	Durham VA ED patients n=134 people (31.8%)	Beers 2003 plus “drug-drug interactions, drug-disease interactions, failure to satisfy an explicit quality indicator” based on published literature	Age, sex, Charlson score, current # of medications, ED visits in the previous year, hospital admissions in the previous year, triage location (ED vs urgent care)	None	Time of ED visit (day vs. night), weekday or weekend visit
Hospital inpatients					
Edwards, 2003 ¹⁹ Retrospective cohort Chart review	Older adult inpatients at a tertiary care teaching hospital 1999–2000	Beers 1997	None	None	Dianosis-Independent Criteria: Number of high severity PIMs on admission-ACE unit (ref: General

Author, Year Study Design Data Source	Population n = Observations of PIM Events	Criteria for PIM	Patient Factors	Clinician factors	System/Environmental Factors
	n=11% of 176 participants in the ACE unit received a high severity PIM, 33.5% received a low severity PIM n=12.7% of 173 participants on general ward received a high severity PIM and 30.1% received a low severity PIM				Medical Unit , number of low severity PIMs on admission, number of medications (high severity and low severity examined separately) prescribed during admission, number of medications (high and low severity examined separately) prescribed at discharge, average change in high- and low-severity PIMs greater in ACE unit (ref: General Medical Unit) Diagnosis-Dependent Criteria: number of PIMs (high and low severity) on admission, number prescribed a PIM (high and low severity) during admission, average change in number of PIMs (high and low-severity)
Schmader, 2004 ²⁰ RCT Medical records	Frail VA patients >65 years hospitalized at 11 VA hospitals n not reported	Medication Appropriateness Index	None	Type of inpatient care (geriatric v. usual) [usual higher, ref: geriatric care] type of outpatient care (geriatric v. usual) [usual inpatient unit care effect in outpatient unit, higher # of inappropriate meds]	None
Hanlon, 2004 ²¹ Cross-sectional secondary analysis of RCT Data originally from medical records, patient report	Random sample of frail VA patients >65 years hospitalized at 11 VA hospitals n= 2796 drugs (78%) n=397 patients (92%)	Medication Appropriateness Index, used by physician-pharmacist pairs	Age, sex, race, marital status, education, employment status, charlson comorbidity [increased] , needing help with ADLs, self rated health [fair/poor, ref: excellent/very good/good] , falls, depression, malnutrition, # of RX meds [increased] , # of non-RX meds [increased]	Admitting specialty (surgery vs. medicine)	None
Linblad, 2005 ²² Cross-sectional secondary analysis of RCT Data originally from medical records, patient report	Random sample of frail VA patients >65 years admitted to one of 11 VA hospitals n=397 persons (40.1%)	Combined McLeod and Beers 1997 criteria focusing on drug-disease interaction	Age [75+, ref: 65-74] , race, sex, marital status [married, ref: other] , education, charlson comorbidity [increased] , ADL difficulty, self-rated health, depression, >1 fall in last 3 months, malnutrition, # of prescription drugs [5+, ref: 1-4]	None	None

Author, Year Study Design Data Source	Population n = Observations of PIM Events	Criteria for PIM	Patient Factors	Clinician factors	System/Environmental Factors
Hajjar, 2005 ²³ Cross-sectional Data originally from medical records, patient report	Random sample of frail VA patients >65 years admitted to one of 11 VA hospitals - n= 384 persons (44%)	Medication Appropriateness Index	4 medications , # of non- prescription drugs Age, sex, race, marital status, education, employment status, charlson comorbidity, depression, malnutrition, HTN [absent, ref: present], angina/ CAD, osteoarthritis, anemia, self-rated health; needing help with 1 or more ADLs, # of prescription medications [9+, ref: 1–4 and 5–8], Multiple prescribers [more than 1 prior to admission, ref: 1 prescriber]	Admitting specialty None	None
Bonk, 2006 ²⁴ Cross-sectional Retrospective Clinical Data Base of Academic health centers	Patients >65 years discharged from one of 40 academic health centers in 2004 n=68,550 (30.2%) received one PIM n= 43,906 (19.4%) received two or more PIMs	Beers 2003 with some drugs excluded if database could not derive route of admin or duration of use	Mean LOS in ICU [more], Mean LOS Inpatient [more], mortality	None	Geographic region
Rothberg, 2008 ²⁵ Retrospective cohort Premier, Inc. Hospitals, Perspective database	Inpatients >65 hospitalized at one of 384 Premier hospitals between 2002–2005 n= 49% of 493,971 patients	Beers 2002 excluding those to be avoided in certain conditions	Age [65–74, ref: 85+], sex [female], race [black, Hispanic, Asian/pacific islander, other, ref: white], marital status [married, ref: not married], principal diagnosis [pneumonia, ref: COPD, chest pain, ischemic stroke] [primary dx CHF, acute MI, UTI, ref: pneumonia] comorbidities [CLD, FEN disorder, anemia, CHF, hypothyroidism, PVD, depression, renal failure, obesity] [absence of HTN and neurological disorders], length of stay	Attending physician specialty, presence of geriatricians [no geriatrician present, ref: present]	Geographic region of hospital [S or W, ref: MW] [MW, ref: NE], insurance status [not managed care, ref: managed care], discharge status, readmission rate, total costs, bed size of hospital [200–400 beds or 400+ beds, ref: 22–200 beds], urban v rural setting, teaching status,
Hale, 2008 ²⁶ Retrospective cohort Chart review	Inpatients >65 at a 760-bed tertiary care teaching hospital 2006 n=39 (39%) patients on admission, 59 (59%) patients during hospitalization, 41 (41%) patients on d/c, 107 PIMs in the hospital	Beers 2003	None	None	Number of PIM at home v. number of PIM at hospital admission; number of PIM at home v. number of PIM at discharge
Ramaswamy, 2010 ²⁷ Survey	Theoretical/vignette patient	None	None	Study only included physician reported barriers to	None

Author, Year Study Design Data Source	Population n = Observations of PIM Events	Criteria for PIM	Patient Factors	Clinician factors	System/Environmental Factors
3 teaching hospitals internal medicine and family medicine residents and attending, geriatrics and sports medicine fellows in the NE/ mid-Atlantic area				appropriate prescribing; Patient taking too many medications was #1, lack of formal education was reported by 72% of residents but 32% of attending, other reported barriers included: cost to patient (89%), potential drug interactions (87%), limited options on insurance formularies (85%), lack of time in office schedule (67%), difficulty communicating with other doctors (61%), lack of information about patient's present medications (60%), lack of formal education on prescribing for the elderly (54%), lack of acceptable therapeutic alternatives (47%), patient's request to maintain a specific medication (41%), unwillingness to discontinue a medication started by another provider (34%), patient's request to begin a specific medication (26%), lack of access to pharmacist (16%)	
Finlayson, 2011 ²⁸ Retrospective cohort Perspective database of Premier hospitals	Elective surgery patients >65 years at one of 379 hospitals participating in the Perspective Database (2006–2008) n= 150,473 persons (55.3%)	Zahn criteria	Age [65–69, ref: 70+], sex [female], race/ethnicity [white, ref: black, hispanic], type of operation, comorbid COPD [COPD present, ref: absent], comorbid CHF [CHF present, ref: absent], comorbid valvular	Specialty of attending physician (General surgery, urology, GYN, orthopedic surgery, other)[orthopedic surgery, ref:	geographical region of hospital [S or W, ref: NE], rural/urban location of hospital, teaching status of hospital

Author, Year Study Design Data Source	Population n = Observations of PIM Events	Criteria for PIM	Patient Factors	Clinician factors	System/Environmental Factors
			disease, comorbid pulmonary circulation disease, comorbid HTN, comorbid rheumatoid disorder [rheumatoid disorder present, ref: absent] , comorbid neurological disease, comorbid PVD, comorbid hypothyroidism, comorbid coagulopathy, comorbid metastatic cancer, comorbid DM [DM absent, ref: present] , comorbid renal failure, comorbid blood loss anemia, comorbid deficiency present, ref: absent] , comorbid psychosis [psychosis present, ref: absent]	general surgery], Consultant (nonsurgical consultant or other/no consultant)[non-surgical consultant involved, ref: general surgery specialty without consultant]	
Morandi, 2013 ²⁹ Prospective Cohort Patient evaluation by trained research personnel (CAM-ICU) and Medical Chart data abstraction - part of larger prospective study (NCT00392795)	Adults in ICU >60 yrs at a tertiary care academic medical center n=250 PIMS at discharge from hospital (to 120 persons) n= 157 pre-admission to hospital (to 120 persons)	Beers 2003 plus "additional medications identified by reviewing the medication safety literature published since 2003" to determine "actually inappropriate medications" based on clinical conversation	Age, sex, race, APACHE-II score, ICU admission diagnosis, comorbidities (charlson) at enrollment, Delirium (CAM-ICU) duration, length of stay, d/c location (home v other) [non-home, ref: home], # pre-admission PIMs [higher]	Discharging service [surgical, ref: medical]	type of ICU at admission
Lund, 2015 ³⁰ Retrospective cohort Centers for Medicare Services Chronic Condition Warehouse - enrollment, claims, part D	Medicare beneficiaries >66 hospitalized for AMI in 2007 or 2008 n= 9607 persons (7.7%) at admission n= 10654 at discharge (8.6%) (4666 new)	HEDIS 2011	None	None	Short term changes: PIM use at admission, PIM started during hospitalization, PIM discontinued during hospitalization, PIM use at d/c [higher, ref, PIM use at admission] *when propoxyphene was excluded PIM use at d/c significantly decreased from admission *when looking only at PIMs with cardiotoxicity their use significantly decreased from admission to d/c Long term changes: PIM use 6 months pre-hospitalization, PIM use 6-months post hospitalization [higher, ref, PIM use at admission] *when propoxyphene excluded still a significant increase at 6 months post *when looking at PIMs with cardiotoxicity they significantly decreased at 6 months post Region: PIM use at admission in each regional area: PIM started

Author, Year Study Design Data Source	Population n = Observations of PIM Events	Criteria for PIM	Patient Factors	Clinician factors	System/Environmental Factors
					during admission, PIM discontinued during hospitalization, PIM use at d/c in each area, PIM use 6 months pre-hospitalization, PIM use 6 months post-hospitalization, [at all time points PIM use highest in South>Midwest> West >Northeast]

Bold – significant factors

ACE = Acute Care for Elders, ADL = Activities of daily living, CIRS-G = The Cumulative Illness Rating Scale for Geriatrics, CV = Cardiovascular, DM = Diabetes mellitus, DNH = Do-Not-Hospitalize, DNR = Do-not-resuscitate, FTE = Full-time equivalent per resident, HMO = Health Maintenance Organization, HEDIS= Healthcare Effectiveness Data and Information Set, ICU = Intensive care unit, LOS = Length of stay, LPN = Licensed practical nurse, MDS = Minimum Data Set, MSA = Metropolitan statistical area, NH = Nursing home, NP = nurse practitioner, OTC = Over-the-counter, RN = Registered nurse, CNA =certified nursing assistant, VA= Veterans Affairs