JAMDA 17 (2016) 862.e1–862.e9

JAMDA

journal homepage: www.jamda.com

Review Article

Prevalence of Potentially Inappropriate Medication Use in Older Adults Living in Nursing Homes: A Systematic Review

Lucas Morin MS [a,*], Marie-Laure Laroche MD, PhD [b,c], Géraldine Texier MD [d], Kristina Johnell MScPharm, PhD [a]

[a] Aging Research Center, Karolinska Institutet and Stockholm University, Stockholm, Sweden
[b] University Hospital of Limoges, Service de Pharmacologie, Toxicologie et Pharmacovigilance, Limoges, France
[c] Université de Limoges, Faculté de Médecine, Limoges, France
[d] University Hospital of Rennes, Palliative Care Support Team, Rennes, France

Keywords:
Inappropriate prescribing
older adults
nursing home
pharmacoepidemiology

A B S T R A C T

Importance: As older adults living in nursing homes are at a high risk of adverse drug-related events, medications with a poor benefit/risk ratio or with a safer alternative should be avoided.
Objectives: To systematically evaluate the prevalence of potentially inappropriate medication use in nursing home residents.
Evidence review: We searched in PubMed and EMBASE databases (1990–2015) for studies reporting the prevalence of potentially inappropriate medication use in people ≥60 years of age living in nursing homes. The risk of bias was assessed with an adapted version of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist.
Findings: A total of 91 articles were assessed for eligibility, and 48 met our inclusion criteria. These articles reported the findings from 43 distinct studies, of which 26 presented *point prevalence* estimates of potentially inappropriate medication use (227,534 nursing home residents). The overall weighted point prevalence of potentially inappropriate medication use in nursing homes was 43.2% [95% confidence interval (CI) 37.3%–49.1%], increasing from 30.3% in studies conducted during 1990–1999 to 49.8% in studies conducted after 2005 ($P < .001$). Point prevalence estimates reported in European countries were found to be higher (49.0%, 95% CI 42.5–55.5) than those reported in North America (26.8%, 95% CI 16.5–37.1) or in other countries (29.8%, 95% CI 19.3–40.3). In addition, 18 studies accounting for 326,562 nursing home residents presented 20 distinct period prevalence estimates ranging from 2.3% to 50.3%. The total number of prescribed medications was consistently reported as the main driving factor for potentially inappropriate medications use.
Conclusions and relevance: This systematic review shows that almost one-half of nursing home residents are exposed to potentially inappropriate medications and suggests an increase prevalence over time. Effective interventions to optimize drug prescribing in nursing home facilities are, therefore, needed.

The number of nursing home residents is rising in most high-income countries.[1] In the United States, the number of nursing home residents has increased from 1.1 to 1.4 million between 1977 and 2013.[2,3] The high prevalence of chronic multimorbidity and symptoms in this population of frail elderly individuals leads to complex medication regimens and to excessive polypharmacy.[4] A recent systematic review showed that up to 74% of nursing home residents were exposed to 10 or more drugs.[5] Because of age-related physiological changes, older adults are at substantially higher risk of adverse drug-related events (eg, gastrointestinal bleedings, impaired cognitive function, injurious falls, and even mortality).[6,7] Optimizing drug prescriptions in nursing homes is, therefore, essential. Medications are considered as potentially inappropriate for use in older people when the risk of harmful effects exceeds their expected benefit for the patient or when a safer, better tolerated or more effective alternative drug is available.[8] Since the landmark initiative from Beers et al in 1991,[9] several tools have been developed to help physicians identify these potentially inappropriate medications.[10,11] In the community setting, 2 systematic

This work was supported by a grant from Forte (2014-4699).
The authors declare no conflicts of interest.
* Address correspondence to Lucas Morin, MS, Aging Research Center, Karolinska Institutet, 113 30 Stockholm, Gävlegatan 16, Sweden.
E-mail address: lucas.morin@ki.se (L. Morin).

http://dx.doi.org/10.1016/j.jamda.2016.06.011

reviews have reported an overall rate of potentially inappropriate medication use of about 20%.[12,13] In contrast, despite serious concern about the poor outcomes associated with inappropriate drug prescribing in nursing homes,[14] no systematic review has been conducted on the institutionalized elderly. Yet, a comprehensive and comparative overview of this issue is necessary to inform clinicians, nursing home directors, and long-term care policy makers.

This systematic review aimed to investigate the prevalence of potentially inappropriate medication use in nursing home residents and to explore variations across geographic areas, time periods, and sets of criteria.

Methods

Design

We conducted a systematic review of the published literature. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist is available in Table A1 (Appendix).

Search Strategy

We searched in PubMed and EMBASE databases for relevant articles published between January 1990 and December 2015, using a combination of keywords and medical subject heading terms (Table A2 in Appendix). We limited our search to articles in English, French, German, or Swedish. The final literature search was performed on December 1, 2015. In addition, the reference lists of included articles were screened manually to identify potentially relevant studies.

Eligibility Criteria

Original studies were included if they reported the prevalence of medications explicitly considered as potentially inappropriate, in people ≥60 years of age living in nursing homes, regardless of the criteria used to assess drug inappropriateness. Studies published before 1990, investigating exclusively community or hospital settings, focusing on a single medication or medication group (eg, benzodiazepines), including only older people with specific physical or intellectual conditions (eg, dementia), or reported in non-peer-reviewed publications (eg, government working papers) were excluded. Studies reporting the outcomes of interventions designed to reduce inappropriate medication use and studies with a sample size <50 individuals were also excluded, as they cannot provide representative prevalence estimates.

Screening and Study Selection

The title and abstract of retrieved articles were first screened by 2 investigators (L.M. and K.J.), with predefined eligibility and exclusion criteria. Duplicates were removed. The full-text copies of potentially relevant articles were then reviewed for inclusion. Any disagreement or uncertainty regarding the eligibility of an article was discussed until a consensus was reached.

Quality Assessment of Studies

The risk of bias in the included studies was assessed by 2 investigators (L.M. and G.T.) with an adapted version of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist[15] (Table A3 in Appendix). Articles were given quality scores ranging from 0 (lowest possible score) to 30 (highest possible score), and were accordingly classified as high (≥25), moderate (20–24), low (15–19), or very low (<15) quality. Discrepancies between the two reviewers were resolved by consensus.

Data Collection

Data were extracted and entered into a standardized spreadsheet under the following headlines: study characteristics (design, period, country, geographic coverage, data source, inclusion criteria, sample size), study population (sex, age, number of prescribed medications), measurement (point or period prevalence estimates, potentially inappropriate medication assessment criteria), quantitative results (total number of potentially inappropriate medications and number of individuals exposed to at least 1 potentially inappropriate medication), and narrative summary of findings. L.M. extracted all the data, and a second reviewer (M.L.) independently assessed a random sample of 10 articles to check accuracy. Disagreements and uncertainties regarding the data were discussed and resolved by consensus.

Data Synthesis

Prevalence estimates of potentially inappropriate medication use were considered as the main outcome of interest. Thus, results from studies reporting more than 1 estimation method (eg, comparing different criteria) were presented for each estimate separately. However, articles reporting the same estimate for the same study population were merged to avoid potential overlap (ie, "double count" of the same patients by different articles).

Prevalence estimates were calculated as the proportion of nursing home residents exposed to at least 1 potentially inappropriate medication at the time of the data collection (point prevalence estimates) or over the study period (period prevalence estimates). By pooling together point prevalence estimates and using the sample size as a weighting factor in random-effects models with unrestricted maximum likelihood, we modeled an overall average point prevalence rate with its 95% confidence intervals (CI). To explore potential variations, this average estimate was then stratified by geographic area ("European countries," "Northern American countries," and "other countries"), time period ("Before 2000," "2000–2005," and "2006–2014") and set of criteria. To evaluate the influence of each study on the overall prevalence estimate, sensitivity analysis was conducted using the leave-one-out approach. Considering the heterogeneity in follow-up time and the lack of information regarding the length of the exposure to potentially inappropriate medication use, we were not able to compute an average weighted estimate of the period prevalence. All analyses were carried out using the Agency for Healthcare Research and Quality-funded, open-source software Open Meta-Analyst (Center for Evidence-based Medicine, Brown University, Providence, RI).[16]

Results

Review Process

Searches in PubMed and EMBASE databases yielded 1635 unique articles, of which 91 were included in the full-text review process. Of these, 48 articles reporting the results from 43 distinct studies met our inclusion criteria and were, therefore, included (Figure 1).

Characteristics of Included Studies

The included studies reported a total of 64 estimates of the prevalence of potentially inappropriate medication use among a total of 553,814 nursing home residents. As described in Table 1, these studies were conducted in 18 different countries: 12 were conducted in the United States (259,802 residents), 6 in Canada (146,377 residents), 20 in Europe (142,298 residents), and 5 in other countries (5337 residents, including 3343 in Australia). Sixteen studies were conducted between 1990 and 1999, 9 between 2000 and 2005, and 18 between 2006 and 2014. Most studies (n = 32) assessed the use of potentially

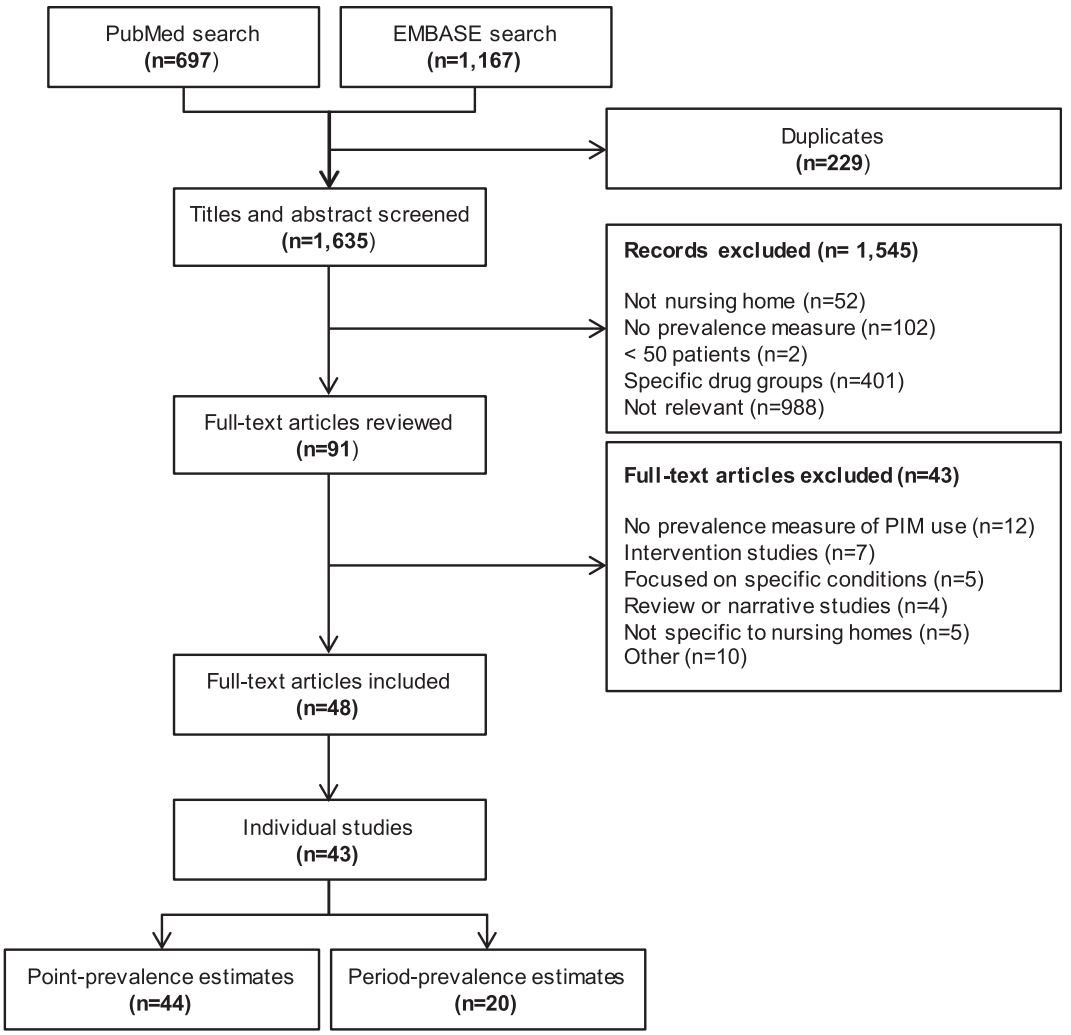

Fig. 1. PRISMA flowchart of the review process. The category "Other" includes 1 study protocol, 3 conference papers, 2 studies about hospitalized individuals, 2 studies focusing on drug-drug interactions, 1 study including only intermediate-care facilities, and 1 study comparing the prescribing patterns of general practitioners and geriatricians.

inappropriate medications cross-sectionally and used medication charts (n = 13), medical records (n = 11), or healthcare databases (n = 15) to collect data (Table 1). The risk of bias is presented for each study in Table A4 in Appendix, and visually represented in a funnel plot of prevalence rate (%) by study population size (Figure A1).

Criteria to Assess Potentially Inappropriate Medication Use

One study used implicit criteria.[34] The 42 other studies used 19 different sets of explicit criteria to measure the prevalence of potentially inappropriate medication use in nursing home residents (Table 1). The different versions of the Beers' criteria were used in 70% (n = 30) studies, Screening Tool of Older Person's Prescriptions (STOPP) criteria were used in seven studies, Laroche's list of criteria in 4 studies, the quality indicators established by the Swedish Board of Health and Welfare in 3 studies, and the Norwegian General Practice (NORGEP) criteria in 2 studies. Other sets of explicit criteria included McLeod (2 studies) and START (4 studies). Eleven articles reported the comparison of ≥2 distinct sets of explicit criteria.

Point Prevalence of Potentially Inappropriate Medication Use

Twenty-six studies reported a total of 44 distinct point prevalence estimates, accounting for 227,534 nursing home residents. As shown in Figure 2, the overall weighted point prevalence of potentially inappropriate medication use in nursing homes was 43.2% (95% CI 37.3%–49.1%). Prevalence estimated ranged from 5.4%[22] to 95%,[33] with sample sizes varying from 50[26] to 86,312[46] residents. Despite a large heterogeneity in study designs, data sources and criteria used to identify potentially inappropriate medications, studies conducted in Europe reported a higher weighted point-prevalence (49.0%, 95% CI 42.5–55.5) than studies conducted in North America (26.8%, 95% CI 16.5–37.1), or in other countries (29.8%, 95% CI 19.3–40.3). Also, compared with studies conducted between 1990 and 1999, studies conducted after 2005 showed a higher weighted point-prevalence rate of potentially inappropriate medication use (49.8% vs 30.3%, $P < .01$). Figure A2 in the Appendix presents the different estimates categorized by criteria. We found that both the overall prevalence and the different area-specific estimates remained stable in the leave-one-out sensitivity analysis (Figure A3 in the Appendix).

Period Prevalence of Potentially Inappropriate Medication Use

Eighteen studies reported 20 distinct period prevalence estimates for a total population of 326,562 nursing home residents (Table 2). The length of the follow-up period varied from 7 to 730 days, although most studies measured the prevalence of potentially inappropriate

Table 1
Characteristics of Included Studies

Author (Year of Publication)	Country	Residents	Nursing Homes	Age	Method of Data Collection	Criteria
		No (% Women)	No	Mean (SD, Range)		
Barnett et al[17] (2011)	Scotland	4557 (72.3%)	NR	84.5 (7.5)	Record-linkage healthcare database	Beers 2003
Beers et al[18] (1992) and Beers et al[19] (1993)	United States	1106 (80%)	12	84.0 (65 to 107)	Medication charts	Beers 1991
Bergman et al[20] (2007)	Sweden	7904 (69.7%)	NR	85.0 (NR)	Record-linkage healthcare database	Swedish criteria
Beuscart et al[21] (2014)	France	9284 (NR)	NR	NR	Administrative data	Laroche
Bronskill et al[22] (2012)	Canada	64,394 (72.5%)	589	84.4 (7.4)	Record-linkage healthcare database	Beers 2003
Chen et al[23] (2012) and Al Aqqad et al[24] (2014)	Malaysia	211 (60.7%)	4	77.7 (7.0)	Medical records and interviews	Beers 2003, STOPP
Chiang et al[25] (2000)	United States	414 (75%)	20	84.0 (NR)	Medication charts	Beers 1991
Conejos-Miquel et al[26] (2010)	Spain	50 (76%)	1	84.5 (7.6)	Medical records	STOPP, START, Beers 2003
Cool et al[27] (2014)	France	974 (71.9%)	175	85.8 (8.4)	Medication charts	Laroche
Dedhiya et al[28] (2010)	United States	7594 (76.5%)	NR	83.1 (6.8)	Administrative data	Beers 2003
Dhall et al[29] (2002)	United States	44,562 (68.7%)	1492	41.2% ≥85 years	SAGE database	Beers 1997
Dhalla et al[30] (2002)	Canada	19,911 (71.8%)	NS	82.6 (7.0)	Administrative data	Beers 1997
Dosa et al[31] (2013)	United States	176,168 (0.4%)	NR	NR	Record-linkage healthcare database	HEDIS
Elseviers et al[32] (2014)	Belgium	1730 (78.1%)	76	84.8 (60 to 104)	Medication charts	ACOVE, Beers 2003, BEDNURS
Garcia-Gollarte et al[33] (2012)	Spain	100 (80%)	6	84.7 (7.5)	Medical records	STOPP, START, Australian criteria
Gill et al[34] (2001)	Canada	355 (NR)	1	79.6 (NR)	Medication charts	Implicit criteria
Gray et al[35] (2003)	United States	282 (73.4%)	NR	82.9 (7.9)	Administrative data and interviews	Beers 1997
Halvorsen et al[36] (2012)	Norway	2986 (71.8%)	NR	85.3 (7.3)	Computerized database	NORGEP
Hosia-Randell et al[37] (2008)	Finland	1987 (80.7%)	20	83.7 (7.7)	Medical records	Beers 2003
King et al[38] (2007)	Australia	998 (71%)	15	83.6 (NR)	Medication charts	Beers 2003
Kölzsch et al[39] (2011)	Germany	8685 (83.7%)	NR	83.6 (7.3)	Medication dispensing database	Laroche
Lane et al[40] (2004)	Canada	58,719 (73.3%)	NR	84.2 (7.5)	Administrative data	Zhan
Lao et al[41] (2013)	China	114 (66.7%)	1	86.6 (8.4)	Medical records	STOPP
Lau et al[42] (2004) and Lau et al[43] (2005)	United States	3372 (73.8%)	NR	49.6% ≥85 years	Administrative data	Beers 1997
Lunn et al[44] (1997)	England	101 (77.2%)	5	85.0 (NR)	Medication charts	Specifically developed criteria
Mann et al[45] (2013)	Austria	1844 (73%)	48	81.0 (12.0)	Medication charts	Austrian criteria
Morin et al[46] (2015) and Haasum et al[47] (2012)	Sweden	86,312 (70.2%)	NR	85.6 (7.2)	Record-linkage healthcare database	Laroche, Beers 2012, NORGEP, PRISCUS, Swedish criteria
Niwata et al[48] (2006)	Japan	1669 (74.3%)	17	84.5 (NR)	Patients files	Beers 2003
Nygaard et al[49] (2003)	Norway	1042 (78%)	15	86.3 (6.8)	Medication charts	BEDNURS, Beers 1997
O'Sullivan et al[50] (2013)	Ireland	732 (70.2%)	14	83.9 (7.7)	Medical records	STOPP, Beers 2003
Papaioannou et al[51] (2002)	Canada	365 (75.6%)	NR	84.2 (8.1)	Administrative data	McLeod
Perri et al[52] (2005)	United States	1117 (81.6%)	15	84.6 (8.08)	Medical records	Beers 1997
Piecoro et al[53] (2000)	United States	20,573 (NR)	NR	NR	Administrative data	Beers 1991
Rancourt et al[54] (2004)	Canada	2633 (74.2%)	29	82.0 (8.0)	Medical records	Rancourt
Ruggiero et al[55] (2010)	Italy	1716 (71.7%)	NR	83.4 (8.1)	InterRAI instrument	Beers 2003
Ruths et al[56] (2008)	Norway	1513 (76%)	23	85.0 (NR)	Medication charts	Swedish criteria
Ryan et al[57] (2013)	Ireland	313 (74.4%)	7	84.4 (7.5)	Patients files	STOPP, START
Shah et al[58] (2012)	England and Wales	10,387 (76.8%)	NR	85.5 (NR)	Record-linkage healthcare database	Beers 2003
Sloane et al[59] (2002) Sloane et al[60] (2004)	United States	2014 (75.8%)	193	52.0% ≥85 years	Survey questionnaire	Beers 1997
Spore et al[61] (1997)	United States	2054 (74.1%)	493	82.0 (65 to 109)	Medication charts	Beers 1991, Stuck
Stafford et al[62] (2011)	Australia	2345 (75.5%)	41	87* (65 to 106)	Medical records	Beers 2003, McLeod
Ubeda et al[63] (2012)	Spain	81 (63%)	1	84.0 (8.0)	Medication charts	Beers 2003, STOPP
Zuckerman et al[64] (2005)	United States	546 (74.7%)	59	81.4 (7.3)	Medication charts	Beers 1997

ACOVE, Assessing Care of Vulnerable Elders; BEDNURS, Bergen District Nursing Home Study; HEDIS, Healthcare Effectiveness Data and Information Set; NORGEP, Norwegian General Practice; SAGE, Systematic Assessment of Geriatric drug use via Epidemiology (PMID: 10026659); START, Screening Tool to Alert doctors to Right Treatment; STOPP, Screening Tool of Older Person's Prescriptions.

*Stafford et al (2011): median age.

medication use over a 1-year (n = 8) or a 3-month (n = 4) period. We found no association between the follow-up time and the prevalence of potentially inappropriate medication use: studies investigating medication use over a 7-day period reported a prevalence ranging from 16.0%[59] to 24.1%,[61] while studies using a 1-year follow-up reported prevalence rates ranging from 2.3%[40] to 50.3%.[42,43]

Factors Associated With Potentially Inappropriate Medication Use

The total number of prescribed medications was the most commonly reported factor associated with an increased likelihood of receiving potentially inappropriate medications.[25,34,35,48–50,52,54,56,57,59,61,63,64] One study also found that

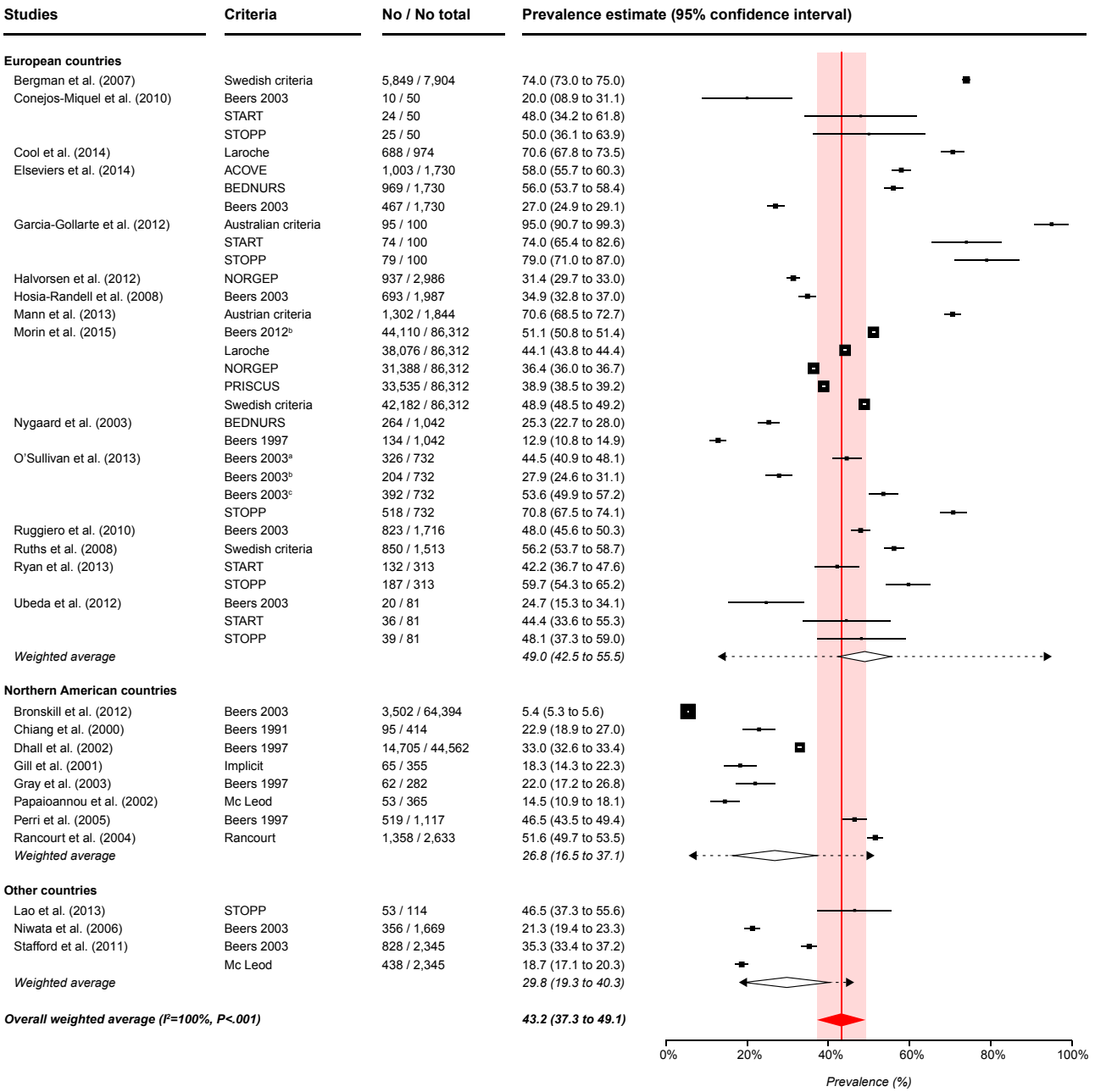

Fig. 2. Point-prevalence of potentially inappropriate medication use in nursing homes, by geographic area. Black squares represent individual estimates. Size is proportional to the number of nursing home residents for which the estimate was calculated. The vertical red line indicates the overall weighted average prevalence rate of potentially inappropriate medications use, while the red diamond and the light-red shade indicate the 95% confidence interval of this overall weighted rate. White diamonds represent the weighted average prevalence estimates (with their 95% CI) for each geographic area. Horizontal dashed lines represent the range between the lowest and the highest estimates for each geographic area. Estimates were calculated using random-effect models with unrestricted maximum likelihood weighting. [a]Diagnosis-dependent criteria only. [b]Diagnosis-independent criteria only. [c]Full set of criteria.

higher facility-level rates of polypharmacy were correlated with the prevalence of potentially inappropriate medication use.[22] Five studies reported that age was negatively correlated with potentially inappropriate medication use,[31,39,45,48,54] 5 studies found that higher age was associated with increased risk of receiving potentially inappropriate medications,[27,30,32,46,47] and 9 studies found no significant association.[34,41–43,50,52,56,57,61] Several studies suggested that cognitive impairment and dementia were associated with a decreased likelihood of receiving potentially inappropriate medications.[29,31,52] One study found that although residents with and without dementia had the same likelihood of receiving potentially inappropriate medications before nursing home admission, residents with dementia were 27% less likely to receive potentially inappropriate medications after nursing home admission.[64]

Drugs Most Frequently Involved in Potentially Inappropriate Medication Use

Long-acting benzodiazepines, fluoxetine, tricyclic antidepressant (eg, amitriptyline), medications with anticholinergic properties (eg, hydroxyzine and oxybutynin), nonsteroidal anti-inflammatory drugs (eg, propoxyphene), digoxin, proton-pump inhibitors, iron

Table 2
Period-Prevalence Estimates of Potentially Inappropriate Medication Use in Nursing Homes

Study (Year of Publication)	Study Design	Time Period Studied	Sample Size	Length of the Study Period	Criteria	Number of Residents with ≥1 PIM
			No Residents	No of Days		No (%)
Barnett et al[17] (2011)	Cohort study	2005 to 2006	4557	730	Beers 2003	1690 (37.1%)
Beers et al[18] (1992)	Cohort study	1990 and 1991	1106	30	Beers 1991	446 (40.3%)
Beuscart et al[21] (2014)	Cross-sectional study	January to March 2012	9284	90	Laroche	3594 (38.7%)
Chen et al[23] (2012)	Cross-sectional study	January to February 2011	211	61	Beers 2003	69 (32.7%)
					STOPP	50 (23.7%)
Dedhiya et al[28] (2010)	Cohort study	2003	7594	365	Beers 2003	3197 (42.1%)
Dhalla et al[30] (2002)	Cohort study	April 1997 to March 1999	19,911	365	Beers 1997	4145 (20.8%)
Dosa et al[31] (2013)	Cross-sectional study	2004 to 2009	176,168	365	HEDIS	28,970 (16.4%)
Gray et al[35] (2003)	Cross-sectional study	April to December 1998	282	365	Beers 1997	121 (42.9%)
King et al[38] (2007)	Cross-sectional study	February to March 1994	998	7	Beers 2003	185 (18.5%)
Kölzsch et al[39] (2011)	Cross-sectional study	April to June 2007	8685	90	Laroche	1903 (21.9%)
Lane et al[40] (2004)	Cohort study	2001	58,719	365	Zhan	1328 (2.3%)
Lau et al[42,43] (2004)	Cross-sectional study	1996	3372	365	Beers 1997	1696 (50.3%)
Lunn et al[44] (1997)	Cross-sectional study	September to November 1993	101	90	Specifically developed criteria	54 (53.5%)
Piecoro et al[53] (2000)	Cross-sectional study	1996	20,573	365	Beers 1991	6830 (33.2%)
Shah et al[58] (2012)	Cross-sectional study	March 2008 to February 2009	10,387	90	Beers 2003	3428 (33%)
Sloane et al[59] (2002) Slone et al[60] (2004)	Cross-sectional study	October 1997 to November 1998	2014	7	Beers 1997	322 (16%)
Spore et al[61] (1997)	Cross-sectional study	July to November 1998	2054	7	Beers 1991	495 (24.1%)
					Stuck	367 (17.9%)
Zuckerman et al[64] (2005)	Cohort study	1992 to 1995	546	365	Beers 1997	242 (44.3%)

PIM, potentially inappropriate medication; STOPP, Screening Tool of Older Person's Prescriptions; HEDIS, Healthcare Effectiveness Data and Information Set.
Spore et al (1997) also used a modified version of the Stuck criteria (n = 365/2054 patients detected). Dedhiya et al (2010) reported the proportion of nursing home residents who received PIM between January and December 2003 after having received no PIM from October 2002 through December 2002. Dhalla et al (2002) reported the prevalence of PIM use both before and after nursing home admission. Considering the aim of this review, we only reported the postadmission estimate.

supplements, ferrous sulfates, and nitrofurantoin were the most commonly reported inappropriate medications (Table A4 in the Appendix).

Discussion

This systematic review suggests that almost one-half of nursing home residents (43%) are exposed to potentially inappropriate medication use, with increasing prevalence estimates between 1990 and 2014. In a recent systematic review, Opondo et al[12] reported an average prevalence of inappropriate prescriptions of 20% among community-dwelling elderly (ie, one-half of our estimate in the nursing home setting).[12] Despite the methodological caveats intrinsic to such comparison, this would suggest that institutionalized older adults are at greater risk of receiving potentially inappropriate medications. The association between the place of residence and the likelihood of being exposed to these medications is, however, subject to conflicting results, with studies reporting significantly higher odds of receiving potentially inappropriate medications for institutionalized elderly compared with community-dwellers,[46,47,53,58] studies reporting no significant association,[17] and studies reporting a decrease after nursing home admission.[40]

A higher number of drugs was reported as the main driving factor for potentially inappropriate medications use. Previous studies and systematic reviews have indeed emphasized the high prevalence of polypharmacy in nursing homes, with up to 74% of residents using 10 different medications or more.[5] Cognitive impairment was, in contrast, often found to be associated with a decrease in the use of potentially inappropriate medications; thus, suggesting a more cautious prescribing approach for this group of particularly frail older adults[65] (although excessive polypharmacy was found to be common among nursing home residents with advanced dementia[66]).

One striking finding of this review is the wide variation between geographic areas: the prevalence of potentially inappropriate medications use seemed to be significantly higher in Europe than in northern American countries. These disparities may be attributable to 4 different factors. First, prior studies suggested that differences in drug availability costs, reimbursement schemes, and purchasing systems were mainly responsible for spatial variation in the quality of drug prescribing.[67] Second, the multidose dispensing system implemented in Nordic European countries has been found to substantially increase the risk of being exposed to potentially inappropriate medications,[68,69] and Scandinavia accounts for a large share of the studies included in this review. Third, discrepancies in the prevalence of inappropriate medications use might stem from differences in the organization of long-term care services across countries,[70,71] leading to significant variation in the burden of chronic diseases of nursing home residents and in the availability of trained geriatricians and pharmacists, which could in turn affect the patterns of medications use.[72–74] Finally, cultural differences in beliefs, attitudes, and practices associated with drug prescribing in frail older adults could partially explain the gap observed in this review between Europe and North America.[75,76] In the United States for instance, the development of regulation and monitoring instruments,[77] the regular update and dissemination of the Beers criteria by the American Geriatrics Society,[78,79] and the implementation of the Choosing Wisely campaign in a large variety of care settings[80] have contributed to raising awareness and concern about the inappropriate use of prescription drugs among healthcare professionals. In Europe, such ambitious initiatives are still lacking, in spite of recent efforts.[9,81,82]

Another important finding is the increasing prevalence of potentially inappropriate medications use over time. Studies conducted before 2005 reported lower estimates than studies conducted afterward. Part of the explanation most likely lies in the evolution of the different explicit criteria, which now include a wider range of medications and may, therefore, artificially inflate the proportion of residents exposed to potentially inappropriate medications. Nonetheless, the absence of a decreasing trend since 1990 should raise concern

among healthcare professionals and policymakers: the accumulation of evidence regarding the adverse outcomes of inappropriate medications use[55,83,84] and the multiplication of validated tools to identify these medications do not seem to have led to any significant improvement in the quality of prescribing in nursing homes.

In fact, no intervention has yet been proven effective in reducing the prescription of inappropriate medications in the long-term care setting, and only a handful of randomized controlled trials have been reported until now.[85] A recent review initiated by the Cochrane Collaboration concluded that medication reviews have resulted in a reduction of inappropriate drug use in all 5 studies meeting the eligibility criteria, but that the level of evidence was, however, too low to draw any robust conclusion.[86] This conclusion is consistent with studies questioning the effectiveness of policy regulation relying solely on the implementation of mandatory medication reviews.[87] Because of the considerable burden of chronic multimorbidity, distressing symptoms, and neuropsychiatric disorders among institutionalized elderly, optimizing medication use in nursing homes is often more complex than in the community setting. The challenge is not only to avoid specific drug classes, but also to find the proper balance between the need for many medications and the potential risk of adverse event that each additional medication introduces. Therefore, without adequately designed interventions to improve the quality of prescribing in nursing homes, the prevalence of inappropriate medications use is unlikely to decrease over the course of the next few years.

The results of this review should be considered in light of several limitations. First, although we used a carefully designed and systematic search strategy, it is possible that studies presenting eligible prevalence estimates were not reviewed. Second, our overall measure of the prevalence of potentially inappropriate medication use is limited in its conclusion by considerable variation between the individual estimates. Also, because of the heterogeneity of the studies included in this review, we could not combine the data in a meta-regression to identify factors associated with higher or lower risks of inappropriate medication use. The large diversity of criteria used in the different studies may also have introduced bias in the overall prevalence estimate (eg, if studies with the largest sample sizes were based on the most extensive criteria). However, a recent country-wide study comparing 5 different sets of criteria found considerable overlap in the prevalence estimates of potentially inappropriate medications use.[46] Third, using the adapted STROBE guidelines, 11 of the 43 included studies were categorized as low or very low quality. Although these studies had small sample sizes (and, therefore, accounted for only a small fraction of the overall estimate), this may have affected the robustness of the data. Finally, this review included studies based on explicit and implicit criteria for potentially inappropriate medications use in older adults. Yet, although these instruments have been found to provide reliable and comparable estimates at the population level, their accuracy and clinical relevance at the patient level has been debated.[46,88,89]

Conclusions

This systematic review provides the first comprehensive evaluation of potentially inappropriate medications use in nursing homes. It shows that the use of potentially inappropriate medications affects almost one-half of all nursing home residents. It also reveals that European countries report the highest prevalence of potentially inappropriate medications use and that no significant decrease seems to have occurred over the past 2 decades. Because inappropriate medications use in frail elderly people leads to severe adverse outcomes and induces a considerable economic burden on our healthcare systems, effective interventions to optimize drug prescribing in nursing home facilities are needed. Future studies should, therefore, be designed to identify the best possible combination of strategies and instruments to reduce the use of inappropriate medications to a minimum.

Acknowledgments

The authors thank Jonas Wastesson, PhD, and Davide L. Vetrano, MD, for their helpful comments on this review.

Supplementary Data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jamda.2016.06.011.

References

1. OECD. Recipients of long-term care. In: Health at a Glance 2013: OECD Indicators. OECD Publishing. p. 178–179. Available at: http://dx.doi.org/10.1787/health_glance-2013-en; 2013. Accessed April 15, 2016.
2. Ness J, Ahmed A, Aronow WS. Demographics and payment characteristics of nursing home residents in the United States: A 23-year trend. J Gerontol A Biol Sci Med Sci 2004;59A:1213.
3. Harris-Kojetin L, Sengupta M, Park-Lee E, et al. Long-Term Care Providers and Services Users in the United States: Data from the National Study of Long-Term Care Providers, 2013–2014, Vol 3. Hyattsville, Maryland: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2016.
4. Moore KL, Boscardin WJ, Steinman MA, Schwartz JB. Patterns of chronic comorbid medical conditions in older residents of U.S. nursing homes: Differences between the sexes and across the agespan. J Nutr Health Aging 2014;18:429–436.
5. Jokanovic N, Tan ECK, Dooley MJ, et al. Prevalence and factors associated with polypharmacy in long-term care facilities: A systematic review. J Am Med Dir Assoc 2015;16:535.e1–535.e12.
6. Mallet L, Spinewine A, Huang A. The challenge of managing drug interactions in elderly people. Lancet 2007;370:185–191.
7. Mangoni AA, Jackson SHD. Age-related changes in pharmacokinetics and pharmacodynamics: Basic principles and practical applications. Br J Clin Pharmacol 2003;57:6–14.
8. Spinewine A, Schmader KE, Barber N, et al. Appropriate prescribing in elderly people: How well can it be measured and optimised? Lancet 2007;370:173–184.
9. Beers MH, Ouslander JG, Rollingher I, et al. Explicit criteria for determining inappropriate medication use in nursing home residents. Arch Intern Med 1991;151:1825–1832. Accessed October 7, 2014.
10. O'Mahony D, O'Sullivan D, Byrne S, et al. STOPP/START criteria for potentially inappropriate prescribing in older people: Version 2. Age Ageing 2015;44:213–218.
11. Chang C-B, Chan D-C. Comparison of published explicit criteria for potentially inappropriate medications in older adults. Drugs Aging 2010;27:947–957.
12. 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:e43617.
13. Tommelein E, Mehuys E, Petrovic M, et al. Potentially inappropriate prescribing in community-dwelling older people across Europe: A systematic literature review. Eur J Clin Pharmacol 2015;71:1415–1427.
14. Morley JE. Inappropriate drug prescribing and polypharmacy are major causes of poor outcomes in long-term care. J Am Med Dir Assoc 2014;15:780–782.
15. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. Lancet 2007;370:1453–1457.
16. Wallace BC, Schmid CH, Lau J, Trikalinos TA. Meta-analyst: Software for meta-analysis of binary, continuous and diagnostic data. BMC Med Res Methodol 2009;9:80.
17. Barnett K, McCowan C, Evans JMM, et al. Prevalence and outcomes of use of potentially inappropriate medicines in older people: Cohort study stratified by residence in nursing home or in the community. BMJ Qual Saf 2011;20:275–281.
18. Beers MH, Ouslander JG, Fingold SF, et al. Inappropriate medication prescribing in skilled-nursing facilities. Ann Intern Med 1992;117:684–689.
19. Beers MH, Fingold SF, Ouslander JG, et al. Characteristics and quality of prescribing by doctors practicing in nursing homes. J Am Geriatr Soc 1993;41:802–807.
20. Bergman A, Olsson J, Carlsten A, et al. Evaluation of the quality of drug therapy among elderly patients in nursing homes. Scand J Prim Health Care 2007;25:9–14.
21. Beuscart J-B, Dupont C, Defebvre M-M, Puisieux F. Potentially inappropriate medications (PIMs) and anticholinergic levels in the elderly: A population based study in a French region. Arch Gerontol Geriatr 2014;59:630–635.
22. Bronskill SE, Gill SS, Paterson JM, et al. Exploring variation in rates of polypharmacy across long term care homes. J Am Med Dir Assoc 2012;13:309.e15–309.e21.

23. Chen LL, Tangiisuran B, Shafie AA, Hassali MAA. Evaluation of potentially inappropriate medications among older residents of Malaysian nursing homes. Int J Clin Pharm 2012;34:596–603.
24. Al Aqqad SMH, Chen LL, Shafie AA, et al. The use of potentially inappropriate medications and changes in quality of life among older nursing home residents. Clin Interv Aging 2014;9:201–207.
25. Chiang L, Hirsch SH, Reuben DB. Predictors of medication prescription in nursing homes. J Am Med Dir Assoc 2000;1:97–102.
26. Miquel C, Sánchez Cuervo M, Delgado Silveira E, et al. Potentially inappropriate drug prescription in older subjects across health care settings. Eur Geriatr Med 2010;1:9–14.
27. Cool C, Cestac P, Laborde C, et al. Potentially inappropriate drug prescribing and associated factors in nursing homes. J Am Med Dir Assoc 2014;15:850.e1–850.e9.
28. Dedhiya SD, Hancock E, Craig BA, et al. Incident use and outcomes associated with potentially inappropriate medication use in older adults. Am J Geriatr Pharmacother 2010;8:562–570.
29. Dhall J, Larrat EP, Lapane KL. Use of potentially inappropriate drugs in nursing homes. Pharmacotherapy 2002;22:88–96. Accessed September 10, 2014.
30. Dhalla IA, Anderson GM, Mamdani MM, et al. Inappropriate prescribing before and after nursing home admission. J Am Geriatr Soc 2002;50:995–1000. Accessed May 3, 2014.
31. Dosa D, Cai S, Gidmark S, et al. Potentially inappropriate medication use in veterans residing in community living centers: Have we gotten better? J Am Geriatr Soc 2013;61:1994–1999.
32. Elseviers MM, Vander Stichele RR, Van Bortel L. Quality of prescribing in Belgian nursing homes: An electronic assessment of the medication chart. Int J Qual Health Care 2014;26:93–99.
33. Garcia-Gollarte F, Baleriola-Júlvez J, Ferrero-López I, Cruz-Jentoft AJ. Inappropriate drug prescription at nursing home admission. J Am Med Dir Assoc 2012;13:83.e9–83.e15.
34. Gill SS, Misiaszek BC, Brymer C. Improving prescribing in the elderly: A study in the long term care setting. Can J Clin Pharmacol 2001;8:78–83.
35. Gray SL, Hedrick SC, Rhinard EE, et al. Potentially inappropriate medication use in community residential care facilities. Ann Pharmacother 2003;37:988–993.
36. Halvorsen KH, Granas AG, Engeland A, Ruths S. Prescribing quality for older people in Norwegian nursing homes and home nursing services using multidose dispensed drugs. Pharmacoepidemiol Drug Saf 2012;21:929–936.
37. Hosia-Randell HM, Muurinen SM, Pitkälä KH. Exposure to potentially inappropriate drugs and drug-drug interactions in elderly nursing home residents in Helsinki, Finland: A cross-sectional study. Drugs Aging 2008;25:683–692.
38. King MA, Roberts MS. The influence of the Pharmaceutical Benefits Scheme (PBS) on inappropriate prescribing in Australian nursing homes. Pharm World Sci 2007;29:39–42.
39. Kölzsch M, Kopke K, Fischer T, et al. Prescribing of inappropriate medication in nursing home residents in Germany according to a French consensus list: A cross-sectional cohort study. Pharmacoepidemiol Drug Saf 2011;20:12–19.
40. Lane CJ, Bronskill SE, Sykora K, et al. Potentially inappropriate prescribing in Ontario community-dwelling older adults and nursing home residents. J Am Geriatr Soc 2004;52:861–866.
41. Lao CK, Ho SC, Chan KK, et al. Potentially inappropriate prescribing and drug-drug interactions among elderly Chinese nursing home residents in Macao. Int J Clin Pharm 2013;35:805–812.
42. Lau DT, Kasper JD, Potter DEB, Lyles A. Potentially inappropriate medication prescriptions among elderly nursing home residents: Their scope and associated resident and facility characteristics. Health Serv Res 2004;39:1257–1276.
43. Lau DT, Kasper JD, Potter DEB, et al. Hospitalization and death associated with potentially inappropriate medication prescriptions among elderly nursing home residents. Arch Intern Med 2005;165:68–74.
44. Lunn J, Chan K, Donoghue J, et al. A study of the appropriateness of prescribing in nursing homes. Int J Pharm Pract 1997;5:6–10.
45. Mann E, Haastert B, Böhmdorfer B, et al. Prevalence and associations of potentially inappropriate prescriptions in Austrian nursing home residents: Secondary analysis of a cross-sectional study. Wien Klin Wochenschr 2013;125:180–188.
46. Morin L, Fastbom J, Laroche M-L, Johnell K. Potentially inappropriate drug use in older people: A nationwide comparison of different explicit criteria for population-based estimates. Br J Clin Pharmacol 2015;80:315–324.
47. Haasum Y, Fastbom J, Johnell K. Institutionalization as a risk factor for inappropriate drug use in the elderly: A Swedish nationwide register-based study. Ann Pharmacother 2012;46:339–346.
48. Niwata S, Yamada Y, Ikegami N. Prevalence of inappropriate medication using Beers criteria in Japanese long-term care facilities. BMC Geriatr 2006;6:1.
49. Nygaard HA, Naik M, Ruths S, Straand J. Nursing-home residents and their drug use: A comparison between mentally intact and mentally impaired residents. The Bergen district nursing home (BEDNURS) study. Eur J Clin Pharmacol 2003;59:463–469.
50. O'Sullivan DP, O'Mahony D, Parsons C, et al. A prevalence study of potentially inappropriate prescribing in Irish long-term care residents. Drugs Aging 2013;30:39–49.
51. Papaioannou A, Bedard M, Campbell G, et al. Development and use of a computer program to detect potentially inappropriate prescribing in older adults residing in Canadian long-term care facilities. BMC Geriatr 2002;2:5.
52. Perri M, Menon AM, Deshpande AD, et al. Adverse outcomes associated with inappropriate drug use in nursing homes. Ann Pharmacother 2005;39:405–411.
53. Piecoro LT, Browning SR, Prince TS, et al. A database analysis of potentially inappropriate drug use in an elderly medicaid population. Pharmacotherapy 2000;20:221–228. Accessed May 3, 2014.
54. Rancourt C, Moisan J, Baillargeon L, et al. Potentially inappropriate prescriptions for older patients in long-term care. BMC Geriatr 2004;4:9.
55. Ruggiero C, Dell'Aquila G, Gasperini B, et al. Potentially inappropriate drug prescriptions and risk of hospitalization among older, Italian, nursing home residents: The ULISSE project. Drugs Aging 2010;27:747–758.
56. Ruths S. Evaluation of prescribing quality in nursing homes based on drug-specific indicators : The Bergen district nursing home (BEDNURS) study. Nor J Epidemiol 2008;18:173–178.
57. Ryan C, O'Mahony D, Kennedy J, et al. Potentially inappropriate prescribing in older residents in Irish nursing homes. Age Ageing 2013;42:116–120.
58. Shah S, Carey I, Harris T. Quality of prescribing in care homes and the community in England and Wales. Br J Gen Pract 2012;62:329–336.
59. Sloane PD, Zimmerman S, Brown LC, et al. Inappropriate medication prescribing in residential care/assisted living facilities. J Am Geriatr Soc 2002;50:1001–1011. Accessed May 3, 2014.
60. Sloane PD, Gruber-Baldini AL, Zimmerman S, et al. Medication undertreatment in assisted living settings. Arch Intern Med 2004;164:2031–2037.
61. Spore DL, Mor V, Larrat P, et al. Inappropriate drug prescriptions for elderly residents of board and care facilities. Am J Public Health 1997;87:404–409. Accessed May 3, 2014.
62. Stafford AC, Alswayan MS, Tenni PC. Inappropriate prescribing in older residents of Australian care homes. J Clin Pharm Ther 2011;36:33–44.
63. Ubeda A, Ferrándiz L, Maicas N, et al. Potentially inappropriate prescribing in institutionalised older patients in Spain: The STOPP-START criteria compared with the Beers criteria. Pharm Pract (Granada) 2012;10:83–91. Accessed May 3, 2014.
64. Zuckerman IH, Hernandez JJ, Gruber-Baldini AL, et al. Potentially inappropriate prescribing before and after nursing home admission among patients with and without dementia. Am J Geriatr Pharmacother 2005;3:246–254. Accessed May 3, 2014.
65. Johnell K. Inappropriate drug use in people with cognitive impairment and dementia: A systematic review. Curr Clin Pharmacol 2015;10:178–184.
66. Vetrano DL, Tosato M, Colloca G, et al. Polypharmacy in nursing home residents with severe cognitive impairment: Results from the SHELTER study. Alzheimers Dement 2013;9:587–593.
67. Zhang Y, Baicker K, Newhouse JP. Geographic variation in the quality of prescribing. N Engl J Med 2010;363:1985–1988.
68. Johnell K, Fastbom J. Multi-dose drug dispensing and inappropriate drug use: A nationwide register-based study of over 700,000 elderly. Scand J Prim Health Care 2008;26:86–91.
69. Wallerstedt SM, Fastbom J, Johnell K, et al. Drug treatment in older people before and after the transition to a multi-dose drug dispensing system—A longitudinal analysis. PLoS One 2013;8:e67088.
70. Sanford AM, Orrell M, Tolson D, et al. An international definition for "nursing home." J Am Med Dir Assoc 2015;16:181–184.
71. Colombo F, Llena-Nozal A, Mercier J, Tjadens F. Help Wanted? Providing and Paying for Long-Term Care. OECD Health. Paris: OECD Publishing; 2011.
72. Tolson D, Rolland Y, Katz PR, et al. An international survey of nursing homes. J Am Med Dir Assoc 2013;14:459–462.
73. Onder G, Carpenter I, Finne-Soveri H, et al. Assessment of nursing home residents in Europe: The Services and Health for Elderly in Long TERm care (SHELTER) study. BMC Health Serv Res 2012;12:5.
74. Onder G, Liperoti R, Fialova D, et al. Polypharmacy in nursing home in Europe: Results from the SHELTER study. J Gerontol A Biol Sci Med Sci 2012;67:698–704.
75. Tjia J, Gurwitz JH, Briesacher BA. Challenge of changing nursing home prescribing culture. Am J Geriatr Pharmacother 2011;10:37–46.
76. Hughes CM, Donnelly A, Moyes SA, et al. "The Way We Do Things Around Here": An international comparison of treatment culture in nursing homes. J Am Med Dir Assoc 2012;13:360–367.
77. Hughes CM, Roughead E, Kerse N. Improving use of medicines for older people in long-term care: Contrasting the policy approach of four countries. Health Policy 2008;3:e154–e167.
78. Campanelli CM. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2012;60:616–631.
79. American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated Beers criteria for potentially inappropriate medication Use in older adults. J Am Geriatr Soc 2015;63:2227–2246.
80. Vance J. AMDA-choosing wisely. J Am Med Dir Assoc 2013;14:639–641.
81. Vettorazzi S, Pinto Antunes J, Dévé I, et al. Prescription and Adherence to Medical Plans. A Compilation of Good Practices. European Commission DG SANCO, editor. Luxembourg: Publication Office of the European Union. Available at: https://ec.europa.eu/research/innovation-union/pdf/active-healthy-ageing/gp_a1.pdf; 2013. Accessed July 12, 2016.
82. Renom-Guiteras A, Meyer G, Thürmann PA. The EU(7)-PIM list: A list of potentially inappropriate medications for older people consented by experts from seven European countries. Eur J Clin Pharmacol 2015;71:861–875.
83. Cahir C, Bennett K, Teljeur C, Fahey T. Potentially inappropriate prescribing and adverse health outcomes in community dwelling older patients. Br J Clin Pharmacol 2014;77:201–210.
84. Skoldunger A, Fastbom J, Wimo A, et al. Impact of inappropriate drug use on hospitalizations, mortality, and costs in older persons and persons with dementia: Findings from the SNAC Study. Drugs Aging 2015;32:671–678.

85. Kaur S, Mitchell G, Vitetta L, Roberts MS. Interventions that can reduce inappropriate prescribing in the elderly: A systematic review. Drugs Aging 2009; 26:1013–1028.
86. Alldred DP, Kennedy M-C, Hughes C, et al. Interventions to optimise prescribing for older people in care homes. In: Alldred DP, editor. Cochrane Database of Systematic Reviews, Vol 2. Chichester, UK: John Wiley & Sons, Ltd; 2016. p. CD009095.
87. Briesacher B, Limcangco R, Simoni-Wastila L, et al. Evaluation of nationally mandated drug use reviews to improve patient safety in nursing homes: A natural experiment. J Am Geriatr Soc 2005;53:991–996.
88. Brown JD, Hutchison LC, Li C, et al. Predictive validity of the Beers and Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (STOPP) Criteria to detect adverse drug events, hospitalizations, and emergency department visits in the United States. J Am Geriatr Soc 2016;64: 22–30.
89. Blanco-Reina E, Ariza-Zafra G, Ocaña-Riola R, León-Ortiz M. 2012 American Geriatrics Society Beers Criteria: Enhanced applicability for detecting potentially inappropriate medications in European older adults? A comparison with the screening tool of older person's potentially inappropriate prescriptions. J Am Geriatr Soc 2014;62:1217–1223.