



Geriatric emergency department revisits after discharge with Potentially Inappropriate Medications: A retrospective cohort study

Nada Hammouda, MD, MSCR^{a,*}, Carmen Vargas-Torres, MA^a, John Doucette, PhD^b, Ula Hwang, MD, MPH^{c,d}

^a Department of Emergency Medicine, Mount Sinai School of Medicine, New York City, USA

^b Department of Environmental Medicine and Public Health, Mount Sinai School of Medicine, New York City, USA

^c Department of Emergency Medicine, Yale School of Medicine, New Haven, CT, USA

^d Geriatric Research, Education and Clinical Center, James J. Peters VAMC, Bronx, NY, USA.

ARTICLE INFO

Article history:

Received 4 October 2020

Received in revised form 28 January 2021

Accepted 1 February 2021

Keywords:

Geriatrics

Medication Safety

Older Adults

Prescribing

ED Discharge

Emergency Medicine

Beers criteria

ED revisits

Adverse Drug Events

ADE's

Comorbidity

Polypharmacy

ED Prescribing

Guidelines

Potentially Inappropriate Medications

PIMs

Outcomes

Safe Prescribing

Geriatric Emergencies

Quality of Healthcare

ABSTRACT

Objective: To determine whether Potentially Inappropriate Medications (PIMs) prescribed in an academic emergency department (ED) are associated with increased ED revisits in older adults.

Methods: A retrospective chart review of Medicare beneficiaries 65 years and older, discharged from an academic ED (January 2012 – November 2015) with any PIMs versus no PIMs. PIMs were defined using Category 1 of the 2015 Updated Beers criteria. Primary outcomes, obtained from a Medicare database linked to hospital ED subjects, were ED revisits 3 and 30 days from index ED discharge. Adjusted multiple logistic regression was used with entropy balance weighted covariates: Age in years, Gender, Race, Number of discharge medications, Charlson Comorbidity Index (CCI) score, Emergency Severity Index scores (ESI), Chief Complaint, Medicaid status, and prior 90 Day ED visits.

Results: Over the study period, there were a total of 7,591 Medicare beneficiaries 65+ discharged from the ED with a prescription; 1,383 (18%) received one or more PIMs. ED revisits in 30 days were fewer for the PIMs cohort (12% PIMs vs 16% no PIMs, OR 0.79, 95% CI 0.65 – 0.95, P value <0.005). Hospital admissions in 30 days were fewer for the PIMs cohort (4 PIMs vs 7% no PIMs, OR 0.75, 95% CI 0.56 – 1.00, P value <0.005). In addition to PIMs, covariate risk factors associated with ED revisits in 30 days included comorbidity severity, history of prior ED revisits, chief complaint, and Medicaid status. Risk factors associated with hospitalization in 30 days included those plus age and emergency severity index, but not race nor ethnicity.

Conclusions: Patients discharged from the ED receiving potentially inappropriate medications as defined by Category 1 of the 2015 updated Beers criteria had lower odds of revisiting the ED within 30 days of index visit. Sociodemographic factors such as gender and race did not predict ED revisits or hospital admissions. Clinical characteristics predicted ED revisits and hospital admissions, the strongest risk being increasing Charlson Comorbidity Index score followed by triage acuity and chief complaint. Future studies are needed to delineate the implications of our findings.

© 2021 Elsevier Inc. All rights reserved.

1. Introduction

1.1. Background

Potentially Inappropriate Medication (PIMs) prescribing is a global problem for older adults seeking medical attention. Prevalence rates of PIMs prescribing for older adults in the outpatient setting vary from 3% up to 83% [1–13]. In older adults, polypharmacy is correlated with an increased risk for inappropriate prescribing [6,12,14,15]. Fick et al. reported a 14% prevalence of drug-related problems in older adults

receiving PIMs [16]. This is especially noticeable in the emergency department (ED) setting. In a nationwide study of urban ED's, Hustey et al. reported 32% of older adults visiting the ED were actively consuming PIMs, and 13% were discharged with at least one new PIMs [17]. PIMs prescriptions are associated with increased rates of morbidities and mortality when prescribed long-term, including unwanted drug-drug interactions, fluid retention, worsening cardiac functions, and avoidable hospital admissions [18–20].

1.2. Importance

In 1991, a geriatrician named Mark H. Beers led a consensus cohort that published the first list of PIMs commonly prescribed across geriatric

* Corresponding author at: 3 East 101st Street, Box 1620, New York, NY 10029
E-mail address: nada.hammouda@alumni.mssm.edu (N. Hammouda).

practices nationwide. The Beers list is updated every few years [21] and is designed to guide medication prescribing in the inpatient and outpatient geriatric practice and nursing home setting. It is a list of medications that are generally recommended to be avoided in older adults when managing chronic conditions and taken with caution, especially for longer durations [18,16,19]. However, applying the Beers criteria in the ED setting for PIMs may not be applicable, where many drugs are prescribed for shorter courses to treat urgent conditions, intended to resolve within days [22–25].

1.3. Goals of this investigation

To date, very few studies have evaluated the impact of PIMs prescribing for older adults in the ED setting on patient outcomes [17,26,27]. To our knowledge, only two studies have addressed this question in the United States, with inconclusive results on ED PIMs and risk of revisits [20,28]. The goal of our study was to compare older adults discharged from the ED receiving PIMs prescriptions (PIMs cohort) to those not receiving PIMs prescriptions (no PIMs cohort) and determine if there were differences in rates of ED return visits (revisits) and hospital admissions. We hypothesize patient receiving PIMs prescriptions versus those that do not will have a higher or no difference in risk of revisits and hospitalization.

2. Methods

2.1. Study design and setting

This was a retrospective observational cohort study of ED patients at Mount Sinai Hospital in New York, between January 2012 and November 2015 who received a prescription at discharge. We defined an index visit as the first ED visit per unique patient during our study period. The visit had to end with 'Discharged' disposition and at least one medication prescribed from the ED.

2.2. Selection of participants

Patients were Medicare beneficiaries 65 years and older, discharged from the ED receiving at least one prescription. Patients were categorized to the PIMs cohort if at least one of those prescriptions was on Category 1 of the 2015 Beers list of drugs to avoid in all older adults [29]. PIMs were identified using a look-up tool designed as part of a previous study [30]. The look-up tool is an algorithm coded into an Excel sheet. It classifies discharge medications as category 1 PIMs to avoid based on drug name, class, dose, and duration. Qualifiers for certain drugs in category 1 of the Beers list were also coded into the algorithm of the look-up tool. If the algorithm identified a drug name or class with an attached qualifier, it ran the qualifier code on patient data in order to qualify the drug as a PIM [29]. All other patients discharged with a prescription were in the comparison no PIMs cohort. Patient records were linked to Medicare claims data through a Data Use Agreement (DUA # RSCH-2017-50741).

2.3. Data collection and processing

Hospital reports were created from the electronic medical record (Epic, Aurora WI) extracting demographic, clinical, and prescriptions data for all patients 65 years and older discharged from the ED. Data included age, sex, race/ethnicity (white, black, Asian, Hispanic Other), ED arrival date, ED discharge date, triage acuity as the Emergency Severity Index (ESI) score, comorbidity as the Charlson Comorbidity Index (CCI) score [31], the six most common chief complaint categories by frequency (Altered mental status (AMS), difficulty breathing, fall, weakness, psychological, and pain), total number of medications prescribed per visit, ED visits in the preceding 90 days, and Medicaid status as a socioeconomic indicator. ESI was developed specifically for the ED setting

to triage patients based on acuity and urgency for medical attention [32]. CCI is a comorbidity prognostic index incorporating 19 medical conditions and is used to predict 1 year mortality risk based on the weighted cumulative comorbidity of the patient [31]. CCI has been validated for use in the ED setting [33–36]. Medicare outpatient, inpatient, and carrier claims data using Research Identifiable Files were used to identify outcomes of interest up to 30 days after the index ED visit.

Duplicate visits were removed and index ED visits when prescriptions were given at discharge were flagged. Demographic variables were then linked from the Sinai hospital reports, and CCI was calculated at the time of the index ED visits for all patients using ICD-9 diagnoses up to 1-year prior to the index ED visit date [31,37]. All ED revisits and hospital admissions were identified following the index ED visit, specifically within 3 and 30 days.

To evaluate patients who may have had ED revisits or hospital admissions outside of Sinai, Medicare claims data were linked with the Sinai administrative data using patient names, medical record number and beneficiary ID numbers. ED claims were obtained from the Medicare files using ED Revenue Center Codes 0450–0459, and 0981. ED revisits and hospital admissions (anywhere in the United States) were calculated using Medicare data within 3 and 30 days after the index ED discharge.

2.4. Outcome measures

Primary outcomes were any ED revisits in 3 and 30 days post-discharge from the index visit when an ED medication was prescribed. Secondary outcomes were hospital admissions in 3 and 30 days. All outcome measures were calculated as proportions (%) and Odds Ratios (OR) for both comparison PIMs vs. no PIMs cohorts.

2.5. Primary data analysis

Bivariate analyses compared the outcomes of ED revisits and hospital admissions at 3 and 30 days for PIMs and no PIMs cohorts using the Chi-square test of independent proportions. Entropy balance was used to account for differences in patient characteristics associated with the outcomes of ED revisits and hospital admission, and selection bias with receiving PIMs and no PIMs. Entropy balancing is a method that facilitates the creation of comparison groups that have similar covariate distributions. This method makes observed characteristics between two comparison groups as similar as possible based on observed characteristics other than the treatment [38]. Entropy balance allows the creation of comparison between the groups without loss of sample size. Covariates included in entropy balance weighing were: Age in years, Male Sex, Race (White, Black, Asian, Hispanic, Other), Number of Discharge Medications prescribed during the index visit (categorized into 1, 2, 3, 4+ medications), CCI score (CCI 0, CCI 1, CCI 2–3, CCI 4+), ESI (ESI Missing, ESI 1–2, ESI 3, ESI 4–5), Chief Complaint (Altered Mental Status, Difficulty Breathing, Psychological, Falls, Weakness, Pain), Medicaid status, and prior 90 Day ED visits. For covariates with multiple categories, reference categories used in the multivariate regression models were: Other (Race), 1–2 (ESI score), 0 (CCI), and 1 (Number of Discharge Medications). Adjusted multiple logistic regression of these entropy balanced comparison groups was used to test the association of PIMs status and odds of revisiting the ED and hospital admissions in 3 and 30 days.

Prior studies were powered to detect a difference of 20–25% in 30-day ED revisits between the two cohorts [20,28]. A sample size of 47 patients per cohort would be required to detect a difference of 25% in revisits between comparison cohort with 80% power at 95% confidence. We found no prior literature for 3-day ED revisits, so we utilized the same sample size calculation for ED revisits in 3 days.

Data organization, preparation, revisit and hospitalization calculations, and subsequent statistical analyses were performed using SAS University Edition V9.0 and STATA 16; linking of hospital visit data to Medicare claims data and calculation of revisits using Medicare claims

were performed using STATA 16. Percentages were rounded up to integer values, all other results up to two decimal places, except P values smaller than 0.005, which were reported as P value <0.005 . Analyses were unadjusted for repeated testing. This study was approved by Mount Sinai Program for the Protection of Human Subjects and with a data use agreement with Medicare (DUA RSCH-2017-50741).

3. Results

3.1. Characteristics of study subjects

A total of 71,472 older adults (aged 65+) were discharged from the ED during the study period. Of those, 18,011 (25%) patients received a prescription at discharge. After excluding index visits discharged without prescriptions, 10,830 unique patients discharged from the ED with a prescription remained; 7,591 (70%) of these patients were matched to Medicare data, constituting our study cohort. Of those, 1,383 (18%) received PIMs on index discharge. Fig. 1 illustrates the CONSORT flow diagram for this study.

Differences in characteristics between the PIMs and no PIMs cohort prior to entropy balance weighing are provided in Table 1. Of note, prior to entropy balance weighing, the PIMs cohort was younger (mean ages were 74.85 for the PIMs cohort vs 77.50 for the no PIMs cohort, P value <0.005), had fewer males (33% PIMs vs 36% no PIMs, P value 0.01) and fewer comorbidities (CCI score 0 was 69% in the PIMs cohort vs 59% in the no PIMs cohort, P value <0.005). Fig. 2 provides the standardized differences of covariate distributions in the No PIM cohort to those in the PIM cohort before and after entropy balancing, while Table 2 provides the actual covariate distributions in the PIM versus No PIM cohorts before and after entropy balance. After entropy balance was performed, standardized differences between covariate distributions were nearly 0 (nearly identical in both cohorts).

3.2. Main results

When comparing the PIMs versus no PIMs cohorts, there were no differences in ED revisits in 3 days nor hospital admissions in 3 days. ED revisits in 30 days were fewer for the PIMs cohort (12% PIMs vs

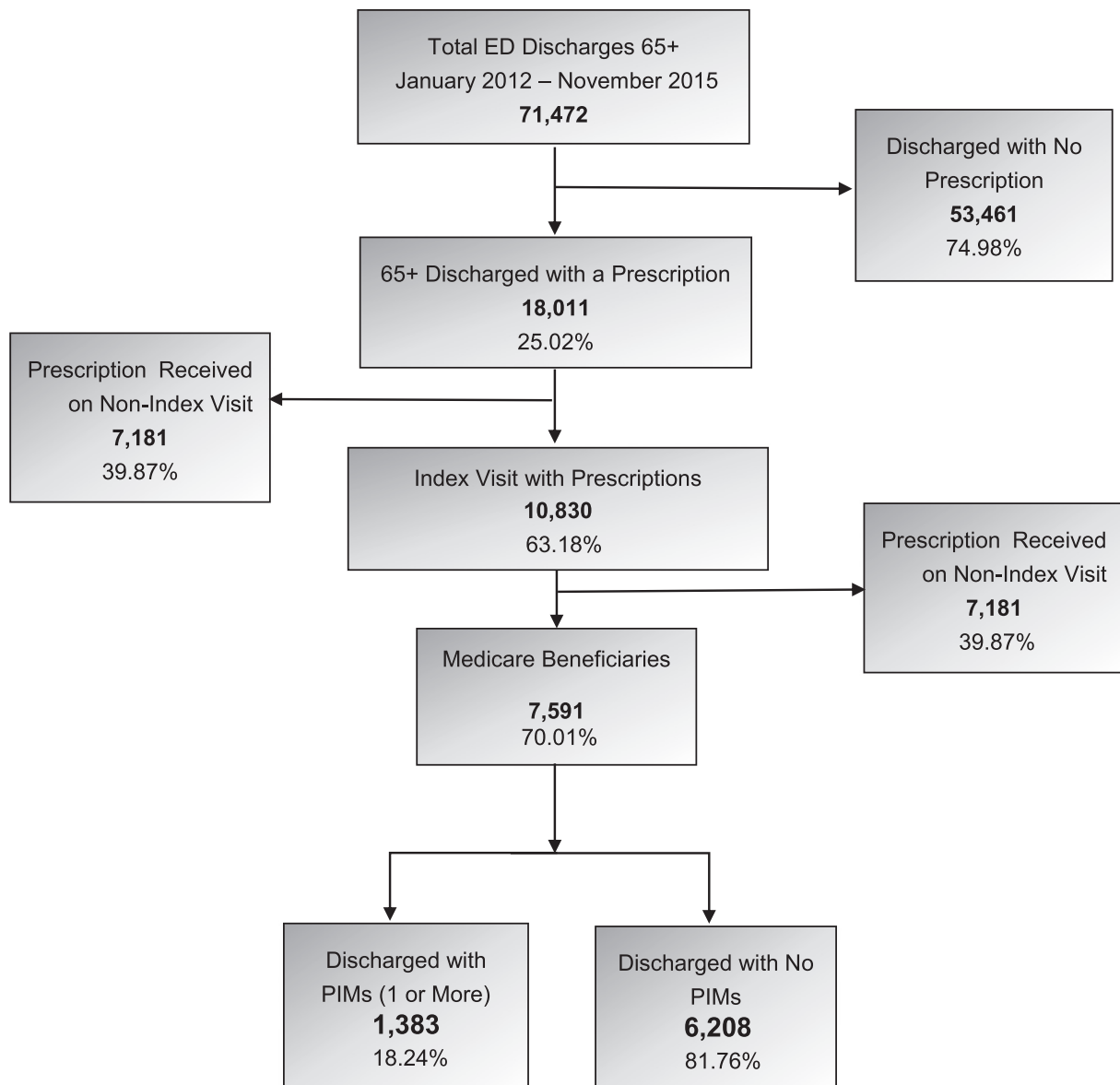


Fig. 1. Study Flow Chart

Table 1

Cohort characteristics prior to entropy balancing and results of their bivariate analyses. Data presented as n (%) unless otherwise indicated. *NA = Not Applicable

	PIM Cohort		No PIM Cohort		P value
	%	n	%	n	
Sample	18	1383	82	6208	NA*
Age mean, SD	74.85	7.72	77.50	8.63	<0.005
Male Gender	33	461	36	2240	0.01
Race					
White	48	670	54	3368	<0.005
Black	32	445	28	1738	<0.005
Asian	2	32	2	120	0.36
Hispanic	13	179	12	731	0.23
Other	4	56	4	241	0.77
ESI Score					
(Missing)	1	7	1	55	NA*
1-2	19	264	24	1482	<0.005
3	62	861	63	3895	0.72
4+	18	251	13	776	<0.005
CCI Score					
0	69	952	59	3686	<0.005
1	11	151	12	765	0.15
2-3	14	197	19	1177	<0.005
4+	6	83	9	580	<0.005
Chief Complaint					
Acute Mental Status	2	23	2	147	0.11
Difficulty Breathing	3	45	6	391	<0.005
Weakness	2	27	4	252	<0.005
Fall	4	59	6	379	<0.05
Psychological	1	14	1	70	0.71
Pain	24	333	13	835	<0.005
Total Discharge Medications					
1	46	633	64	3961	<0.005
2	34	468	25	1579	<0.005
3	12	165	7	418	<0.005
4+	8	117	4	250	<0.005
90 Day Prior ED Visits	12	172	17	1049	<0.005
Medicaid Status	49	677	45	2786	<0.05
ED Revisits					
3 Days	3	36	3	205	0.18
30 Days	12	163	16	985	<0.005
Hospital Admissions					
3 Days	<1	10	<1	42	0.85
30 Days	4	60	7	440	<0.005

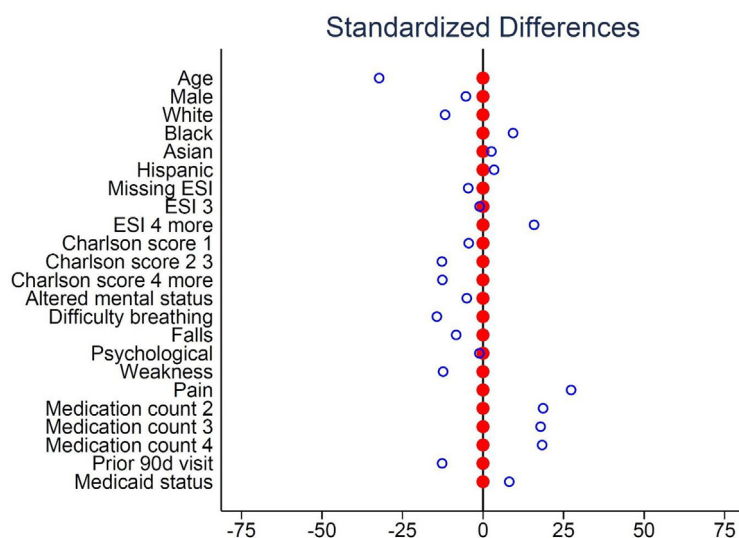
**Fig. 2.** Standardized difference graph of entropy balance-weighted vs non-weighted samples. The blue circles = standardized difference in covariate distribution between PIMs vs No PIMs BEFORE entropy balancing. The red dots = standardized differences AFTER entropy balancing.

Table 2

Comparison of cohort characteristics before and after entropy balance weighting of the No PIM group. Data presented as % unless otherwise indicated.

	PIM Cohort	No PIM Cohort Before Entropy Balance (Unweighted)	No PIM Cohort After Entropy Balance (Weighted)
	%	%	%
Sample	18	82	18
Mean Age (in years)	74.85	77.50	74.86
Male Gender	33	36	33
Race			
White	48	54	48
Black	32	28	32
Asian	2	2	2
Hispanic	13	12	13
Other	4	4	4
ESI Score			
(Missing)	1	1	1
1-2	19	24	19
3	62	63	62
4+	18	13	18
CCI Score			
0	69	59	69
1	11	12	11
2-3	14	19	14
4+	6	9	6
Chief Complaint			
Acute Mental Status	2	2	2
Difficulty Breathing	3	6	3
Weakness	2	4	2
Fall	4	6	4
Psychological	1	1	1
Pain	24	13	24
Total Discharge Medications			
1	46	64	46
2	34	25	34
3	12	7	12
4+	8	4	8
90 Day Prior ED Visits	12	17	12
Medicaid Status	49	45	49

16% no PIMs, OR 0.79, 95% CI 0.65 – 0.95, P value <0.005). Hospital admissions in 30 days were fewer for the PIMs cohort (4% PIMs vs 7% no PIMs, OR 0.75, 95% CI 0.56 – 1.00, P value <0.005). Results of our regression analyses for each separate outcome, along with possible predictors for each outcome, are summarized in [Tables 3 and 4](#).

Additionally, we performed a post-hoc analysis to examine if the covariates ESI and CCI scores confounded or modified the relationship between receiving PIMs and any of our 4 outcomes. We found CCI score was a strong confounder of receiving PIMs and hospital admissions in 3 and 30 days but did not confound receiving PIMs and ED revisits in 3 or 30 days.

4. Discussion

While research has shown that long-term PIMs compounded numerous hazardous outcomes, including increased risks of ED visits and hospital admissions [9,16,39–45], previous studies evaluating PIMs prescribing from the ED had no difference in ED returns or other subsequent outcomes [20,28]. In this cohort, we found ED PIMs prescribing to be associated with a reduced risk of ED revisits within 30 days. These results were surprising as we had hypothesized either an increased risk of ED revisit or no difference for patients prescribed PIMs from the ED, and challenge previously reported findings [31,32].

4.1. Study merits

Although research on PIMs-related adverse drug events (ADE's) is mounting, only three studies reported on PIMs prescribed in the ED [20,28,46]. The studies by Chin [20] and Hastings et al [28] were underpowered to demonstrate an association with adverse outcomes,

including ED returns hospital admissions. Harrison et al found no difference in chief complaint categories nor 7 Day ED revisits in PIMs vs no PIMs [46]. A fourth study, a nationwide database survey by Chen et. al. reported a significant increase in the proportions of ED visits, ambulatory care visits, and hospitalizations in Taiwanese patients receiving PIMs while visiting the ED in 2001–2004 [47]. The covariates included in that analysis were patient, physician, and drug characteristics. However, because of its cross-sectional design, that study did not evaluate the longitudinal outcomes after an index ED discharge. The study simply noted the proportions of each outcome in both cohorts and its cross-sectional designs could not evaluate temporal outcomes.

Ours is the first adequately powered study investigating adverse outcomes of PIMs prescribed in the ED. A larger sample size with 10,000 might have allowed for the ability to detect differences as little as 4% in ED revisits in 3 and 30 days at 90% power and 95% confidence. However, we adjusted for covariates that may have impacted our utilization outcomes, including Age, Race, Gender, Total Discharge Medications, Medicaid status, ESI, CCI, Chief Complaint, and Prior 90 Day ED revisits. Evaluation of outcomes using Medicare claims is a significant strength of this study and allowed us to evaluate returns to a different ED from that of the index visit. With only 36 patients returning to the ED for a revisit in the PIMs cohort, however, we were underpowered to detect a statistically significant difference in ED revisits within 3 days.

As summarized in [Table 1](#), PIMs receivers statistically had fewer comorbidities, were of lower socioeconomic status, needed less urgent attention in the ED, and received multiple medications upon discharge (all P values were <0.005). We suspected those with higher comorbidity and ESI scores would be more likely to return to the ED. Indeed, both ESI and CCI scores were associated with increased ED revisits and hospital admissions. The relationship between comorbidity and hospital

Table 3

Multivariate regression analyses of ED revisits in 3 and 30 days, entropy balance-weighted samples. Data presented as Odds Ratio (95% Confidence Interval). N/A = Not Available. * Patients with Chief Complaint 'Psychological' were dropped from the entropy balance model due to insufficient sample size for this flag. *** p<0.01, ** p<0.05

Covariates for Multivariate Logistic Regression	Outcomes of Multivariate Logistic Regression ED Revisits (n = 7591)			
	30 Days		3 Days	
	OR	95% CI	OR	95% CI
PIMs	0.79	0.65–0.95 **	0.84	0.58–1.23
Age	1.01	1.00–1.02	0.99	0.97–1.02
Male	1.17	0.97–1.41	1.11	0.77–1.60
Race				
White	1.33	0.81–2.21	1.53	0.61–3.83
Black	1.32	0.79–2.19	1.05	0.41–2.68
Asian	0.88	0.38–2.04	1.00	0.22–4.59
Hispanic	0.99	0.57–1.72	0.89	0.31–2.52
ESI Score				
(Missing)	3.73	1.56–8.93 ***	4.75	1.24–18.19 **
3	0.89	0.71–1.12	0.99	0.63–1.56
4+	0.72	0.52–1.00	1.04	0.57–1.90
CCI Score				
1	1.37	1.04–1.81 **	0.94	0.52–1.69
2–3	1.19	0.94–1.51	0.97	0.58–1.62
4+	1.70	1.21–2.38 ***	1.81	0.94–3.48
Chief Complaint				
Altered Mental Status	1.19	0.65–2.19	0.85	0.18–4.12
Difficulty Breathing	1.06	0.68–1.65	1.29	0.57–2.96
Fall	0.89	0.60–1.31	1.13	0.50–2.59
Psychological	0.72	0.30–1.73	0.20	0.05–0.87 **
Weakness	0.78	0.47–1.30	0.92	0.32–2.70
Pain	1.13	0.89–1.42	0.82	0.50–1.36
Total Discharge Medications				
2	0.94	0.78–1.15	1.04	0.70–1.54
3	0.92	0.67–1.25	0.70	0.35–1.37
4+	1.17	0.83–1.66	0.49	0.19–1.25
90 Day Prior ED Visits	1.42	1.13–1.78 ***	1.48	0.93–2.37
Medicaid Status	1.24	1.03–1.49 **	1.20	0.81–1.78

Table 4

Multivariate regression analyses of hospital admissions in 3 and 30 days, entropy balance-weighted samples. Data presented as Odds Ratio (95% Confidence Interval). N/A = Not Available. * Patients with Chief Complaint 'Psychological' were dropped from the entropy balance model due to insufficient sample size for this flag. *** p<0.01, ** p<0.05

Covariates for Multivariate Logistic Regression	Outcomes of Multivariate Logistic Regression Hospital Admissions (n = 7591)			
	3 Days		30 Days	
	OR	95% CI	OR	95% CI
PIMs	1.29	0.62–2.67	0.75	0.56–1.00 **
Age	0.98	0.94–1.03	1.03	1.01–1.05 ***
Male	1.92	0.92–4.01	0.99	0.75–1.32
Race				
White	3.84	0.48–31.00	0.93	0.44–1.96
Black	4.35	0.52–36.43	1.08	0.51–2.30
Asian	7.86	0.43–143.6	0.80	0.21–3.03
Hispanic	4.99	0.57–43.96	0.87	0.38–2.00
ESI Score				
(Missing)	9.88	2.03–48.17 ***	2.48	0.81–7.65
3	0.84	0.39–1.82	0.78	0.57–1.08
4+	0.10	0.01–0.82 **	0.38	0.20–0.71 ***
CCI Score				
1	1.40	0.38–5.15	2.45	1.63–3.69 ***
2–3	1.95	0.61–6.26	2.11	1.49–2.97 ***
4+	4.14	1.43–11.94 ***	3.77	2.47–5.77 ***
Chief Complaint				
Altered Mental Status	2.15	0.31–14.81	1.13	0.56–2.25
Difficulty Breathing	1.72	0.48–6.14	1.50	0.89–2.54
Fall	0.11	0.01–0.86 **	0.82	0.53–1.27
Psychological	N/A	N/A	0.40	0.15–1.08
Weakness	1.90	0.54–6.62	1.15	0.60–2.19
Pain	0.84	0.22–3.14	1.14	0.78–1.68
Total Discharge Medications				
2	0.88	0.35–2.26	0.92	0.68–1.23
3	1.24	0.36–4.26	1.34	0.86–2.08
4+	0.44	0.09–2.11	0.96	0.54–1.69
90 Day Prior ED Visits	2.47	1.12–5.46 **	1.97	1.44–2.69 ***
Medicaid Status	0.98	0.43–2.24	0.83	0.63–1.09

admissions that we uncovered was not entirely surprising as there is mixed evidence in the literature on the link between PIMs and comorbidity [48–50]. However, this meant that PIMs prescribed in the ED may not be associated with risk of subsequent hospital admissions, which is perplexing given prior literature on the hazardous outcomes of PIMs [9,17,32–38]. Future studies should explore the nature and strength of the true association between PIMs, comorbidity, and hospital admissions. While we tried to account for all potential confounders in our study such as ESI and CCI scores, it is possible we may still have undetected clinical variables impacting our results.

If clinical features do not fully explain why fewer patients who received PIM prescriptions revisit the ED or become hospitalized, we may have to look at PIMs from a different angle and reassess our own understanding of their hazards. Growing evidence suggests ED visits and hospitalization rates are associated with the total number of medications prescribed, not PIMs specifically, although we did not find that to be the case [18,27,42,51–58]. Some studies argue that PIMs defined by the STOPP/START criteria, not Beers criteria which were originally developed for use in the nursing home and long-term care setting, increased the risk of unplanned hospitalizations [53,59–67]. Budnitz et al found that many adverse events are related to drugs not on the Beers list, namely insulin regulators, anti-thrombotic, and antiarrhythmic medications [51,68]. Efforts to deprescribe and reduce the risk of negative outcomes should be directed at duration of medication rather than specific drug classes and not potentially inappropriate medications [51,68]. It is possible that patient outcomes may have a greater association with prescription duration rather than it being a potentially inappropriate drug as defined by the Beers criteria. Many of these medications are those that are for longer-term use (i.e., insulin regulators, anti-thrombotic, and antiarrhythmic medications). In contrast, ED prescriptions are typically short-term (a few days up to 1 or 2 weeks) [69]. Long-term use of PIMs may have different outcomes than short-term PIMs, although no current literature exists that compares outcomes from various PIMs durations. A Taiwanese study evaluating outcomes of PIMs and continuity of care in older diabetic patients, Lai and colleagues found increased adverse outcomes correlated with long-term PIMs use beyond 90 and 180 days [18]. Chin et al. suggest PIMs may be appropriately prescribed if used in the short-term [20].

Gender and race had no impact on our utilization outcome results. Contrary to previous reports [19,41–46], sex did not predict ED revisits or hospital admission in 3 and 30 days in our study cohort. For race, we found non-white cohorts were more likely to receive PIMs and more likely to return within 30 days (Table 2). However, race was not associated with ED revisits nor hospital admissions. Furthermore, literature suggests older age may be a stronger predictor of ED revisits than receiving a PIMs [70], but we did not find this to be the case.

4.2. Limitations

Our study has several limitations. This was a single centre study, which limits the generalizability of our results. A strength of our study, however, was the pairing of hospital data with Medicare claims data for the comprehensive evaluation of ED revisit and hospitalization outcomes at any hospital. Our study identified PIMs listed in category 1 of the 2025 updated Beers criteria [29]. We were unable to identify PIMs listed in other categories due to limited time and data. Analysing the impact of prescribing Beers PIMs identified in other categories could have yielded deeper understanding of our study results. We were unable to analyse covariates such as primary and secondary diagnosis (both on index and return visits), or past medical history (PMH). Primary and secondary diagnoses would highlight past ED revisits that were ADE-related. We were also unable to account for prior medication drug history, which would indicate if patients may have already been on long-term PIMs. CCI scores were calculated at the index visit, not at revisits. It is possible patients may have had a change in comorbidity status as a result of the ED visit or even the PIMs. Reasons for visit

may have impacted risk of being prescribed PIMs and impacted patient outcomes. We were unable to analyse prescription refill orders or outpatient visits prior to returning to the ED, or reasons for ED revisits. Our results may not be directly due to PIMs but may have been confounded by refill or dispensing issues in the ED or by outpatient care. Response to PIMs was not further evaluated for the sub-category of the PIMs prescribed, perhaps results would be different under different PIMs categories (Antihistamines, Benzodiazepines, etc.). Our analyses were uncorrected for repeat testing of outcomes on the same study cohort, so the statistically significant p-value threshold remained at 0.05 throughout testing. A Bonferroni correction of the p-value could lead us to re-evaluate the statistical significance of our covariates [71–73]. However, given that most of these covariates' p-values were less than 0.005, it is doubtful their interpretation – or the overall significance of our study – would change. Finally, as an observational study, these findings only demonstrate associations and not causality between ED PIMs prescriptions and fewer returns to the ED.

In summary, patients discharged from the ED receiving potentially inappropriate medications as to avoid using category 1 of the 2015 updated Beers criteria have lower odds of revisiting the ED. This is the first adequately powered study to focus on PIMs prescription in the ED. Future studies should evaluate and account for risks for receiving PIMs, consider how PIMs in the ED may be defined, and investigate the impact of comorbidity and the duration of PIMs prescriptions on adverse health outcomes.

Financial support

This study was a master's thesis project (Hammouda) and not grant funded.

Prior Presentations

Nada Hammouda, Ula Hwang, et al. Risk of Emergency Department Revisit or Hospitalization in Older Adults Discharged with Potentially Inappropriate Medications: A Retrospective Cohort Study. American College of Emergency Physicians (ACEP) 2019 scientific assembly, Denver, CO.

Grant

This study was IRB approved by Mount Sinai Program for the Protection of Human Subjects and through a data use agreement with Medicare (DUA RSCH-2017-50741).

Declaration of Competing Interest

None

Acknowledgements

George Loo, DrPh for his statistical guidance; Rachel Pinotti, MLIS for her assistance in the literature review.

References

- [1] Aguiar JP, Brito AM, Martins AP, Leufkens HGM, Alves da Costa F. Potentially inappropriate medications with risk of cardiovascular adverse events in the elderly: A systematic review of tools addressing inappropriate prescribing. *Review J Clin Pharm Ther.* 2019;44(3):349–60. <https://doi.org/10.1111/jcpt.12811>.
- [2] Akazawa M, Imai H, Igarashi A, Tsutani K. Potentially inappropriate medication use in elderly Japanese patients. *Am J Geriatr Pharmacother.* 2010;8(2):146–60. <https://doi.org/10.1016/j.amjopharm.2010.03.005>.
- [3] Akkawi ME, Nik Mohamed MH, Md Aris MA. Does inappropriate prescribing affect elderly patients' quality of life? A study from a Malaysian tertiary hospital. *Qual Life Res.* 2019. <https://doi.org/10.1007/s11136-019-02153-5>.
- [4] Al Odhayani A, Tourkmani A, Alshehri M, Alqahtani H, Mishriky A. Potentially inappropriate medications prescribed for elderly patients through family physicians. *Saudi J Biol Sci.* 2017;24(1):200–7. <https://doi.org/10.1016/j.sjbs.2016.05.006>.

- [5] Ammerman CA, Simpkins BA, Warman N, Downs TN. Potentially inappropriate medications in older adults: Deprescribing with a clinical pharmacist. *J Am Geriatr Soc*. 2019;67(1):115–8. <https://doi.org/10.1111/jgs.15623>.
- [6] Bao Y, Shao H, Bishop TF, Schackman BR, Bruce ML. Inappropriate medication in a national sample of us elderly patients receiving home health care. *J Gen Intern Med*. 2012;27(3):304–10. <https://doi.org/10.1007/s11606-011-1905-4>.
- [7] Bo M, Quaranta V, Fonte G, Falcone Y, Carignano G, Cappa G. Prevalence, predictors and clinical impact of potentially inappropriate prescriptions in hospital-discharged older patients: A prospective study. *Geriatr Gerontol Int*. 2018;18(4):561–8. <https://doi.org/10.1111/ggi.13216>.
- [8] Castilino RL, Hilmer SN, Bajorek BV, Nishtala P, Chen TF. Drug burden index and potentially inappropriate medications in community-dwelling older people: The impact of home medicines review. *Drugs Aging*. 2010;27(2):135–48. <https://doi.org/10.12165/11531560-000000000-00000>.
- [9] Dalleur O, Spinewine A, Henrard S, Losseau C, Speybroeck N, Boland B. Inappropriate prescribing and related hospital admissions in frail older persons according to the stopp and start criteria. *Drugs Aging*. 2012;29(10):829–37. <https://doi.org/10.1007/s40266-012-0016-1>.
- [10] Danisha P, Dilip C, Mohan PL, Shinu C, Parambil JC, Sajid M. Identification and evaluation of potentially inappropriate medications (pims) in hospitalized geriatric patients using beers criteria. *J Basic Clin Physiol Pharmacol*. 2015;26(4):403–10. <https://doi.org/10.1515/jbcp-2014-0054>.
- [11] Davidoff AJ, Miller GE, Sarpong EM, Yang E, Brandt N, Fick DM. Prevalence of potentially inappropriate medication use in older adults using the 2012 beers criteria. *J Am Geriatr Soc*. 2015;63(3):486–500. <https://doi.org/10.1111/jgs.13320>.
- [12] Gallagher PF, Barry PJ, Ryan C, Hartigan I, O'Mahony D. Inappropriate prescribing in an acutely ill population of elderly patients as determined by beers' criteria. *Age Ageing*. 2008;37(1):96–101. <https://doi.org/10.1093/ageing/afm116>.
- [13] Goltz L, Kullak-Ublick GA, Kirch W. Potentially inappropriate prescribing for elderly outpatients in Germany: a retrospective claims data analysis. *Int J Clin Pharmacol Ther*. 2012;50(3):185–94. <https://doi.org/10.5414/cp201441>.
- [14] Chang CB, Yang SY, Lai HY, et al. Application of three different sets of explicit criteria for assessing inappropriate prescribing in older patients: A nationwide prevalence study of ambulatory care visits in taiwan. *BMJ open*. 2015;5(11):e008214. <https://doi.org/10.1136/bmjopen-2015-008214>.
- [15] Galán Retamal C, Garrido Fernández R, Fernández Espínola S, Ruiz Serrato A, García Ordóñez MA, Padilla Marín V. Prevalence of potentially inappropriate medication in hospitalized elderly patients by using explicit criteria. *Farm Hosp*. 2014;38(4):305–16. <https://doi.org/10.7399/FH.2014.38.4.1148>.
- [16] Fick DM, Mion LC, Beers MH, Waller JL. Health outcomes associated with potentially inappropriate medication use in older adults. *Res Nurs Health*. 2008;31(1):42–51. <https://doi.org/10.1002/nur.20232>.
- [17] Hustey FM, Wallis N, Miller J. Inappropriate prescribing in an older ed population. *Am J Emerg Med*. Sep 2007;25(7):804–7. <https://doi.org/10.1016/j.ajem.2007.01.018>.
- [18] Lai YR, Yang YS, Tsai ML, et al. Impact of potentially inappropriate medication and continuity of care in a sample of taiwan elderly patients with diabetes mellitus who have also experienced heart failure. *Geriatr Gerontol Int*. Oct 2016;16(10):1117–26. <https://doi.org/10.1111/ggi.12606>.
- [19] Patel R, Zhu L, Sohal D, et al. Use of 2015 beers criteria medications by older medicare beneficiaries. *Consult Pharm*. 2018;33(1):48–54. <https://doi.org/10.4140/TCPh.n.2018.48>.
- [20] Chin MH, Jin L, Karrison TG, et al. Older patients' health-related quality of life around an episode of emergency illness. *Ann Emerg Med*. 1999;34(5):595–603.
- [21] 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. *Arch Intern Med*. Dec 8 2003;163(22):2716–24. <https://doi.org/10.1001/archinte.163.22.2716>.
- [22] Butler MM, Ancona RM, Beauchamp GA, et al. Emergency department prescription opioids as an initial exposure preceding addiction. *Ann Emerg Med*. 2016;68(2):202–8. <https://doi.org/10.1016/j.annemergmed.2015.11.033>.
- [23] Gallagher P, Lavan A, O'Mahony D. Prescribing for older patients. In: Nickel C, Bellou A, Conroy S, editors. *Geriatric emergency medicine*. Springer International Publishing; 2018. p. 299–313.
- [24] Sanders AEPAB. *Drug therapy in the geriatric patient*. 9th ed. Elsevier, Inc.; 2018: 2334–2340.
- [25] Jeffrey J, Schaidler, Roger M. Barkin, Philip Shayne, Richard E. Wolfe, Stephen R. Hayden, Peter Rosen. *Rosen & barkin's 5-minute emergency medicine consult Standard ed*.
- [26] Hustey FM. Beers criteria and the ed: An adequate standard for inappropriate prescribing? *Am J Emerg Med*. Jul 2008;26(6):695–6. <https://doi.org/10.1016/j.ajem.2008.01.008>.
- [27] Caterino JM, Emond JA, Camargo Jr CA. Inappropriate medication administration to the acutely ill elderly: A nationwide emergency department study, 1992–2000. *J Am Geriatr Soc*. Nov 2004;52(11). <https://doi.org/10.1111/j.1532-5415.2004.52503.x> 1847–55.
- [28] Hastings SN, Schmadre KE, Sloane RJ, et al. Quality of pharmacotherapy and outcomes for older veterans discharged from the emergency department. *J Am Geriatr Soc*. May 2008;56(5):875–80. <https://doi.org/10.1111/j.1532-5415.2008.01648.x>.
- [29] Samuel MJ. American geriatrics society 2015 updated beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2015;63(11):2227–46. <https://doi.org/10.1111/jgs.13702>.
- [30] Stevens M, Hastings SN, Markland AD, et al. Enhancing quality of provider practices for older adults in the emergency department (equipped). *J Am Geriatr Soc*. Jul 2017;65(7):1609–14. <https://doi.org/10.1111/jgs.14890>.
- [31] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J Chronic Dis*. 1987;40(5):373–83. [https://doi.org/10.1016/0021-9681\(87\)90171-8](https://doi.org/10.1016/0021-9681(87)90171-8).
- [32] Singer RF, Infante AA, Oppenheimer CC, West CA, Siegel B. The use of and satisfaction with the emergency severity index. *J Emerg Nurs*. Mar 2012;38(2):120–6. <https://doi.org/10.1016/j.jen.2010.07.004>.
- [33] Wang HY, Chew G, Kung CT, Chung KJ, Lee WH. The use of charlson comorbidity index for patients revisiting the emergency department within 72 hours. *Chang Gung Med J Sep-Oct*. 2007;30(5):437–44.
- [34] Murray SB, Bates DW, Ngo L, Ufberg JW, Shapiro NI. Charlson index is associated with one-year mortality in emergency department patients with suspected infection. *Acad Emerg Med*. May 2006;13(5):530–6. <https://doi.org/10.1197/j.aem.2005.11.084>.
- [35] Bahrmann A, Benner L, Christ M, et al. The charlson comorbidity and barthel index predict length of hospital stay, mortality, cardiovascular mortality and rehospitalization in unselected older patients admitted to the emergency department. *Aging Clin Exp Res*. Sep 2019;31(9):1233–42. <https://doi.org/10.1007/s40520-018-1067-x>.
- [36] Çildir E, Bulut M, Akalin H, Kocabaş E, Ocakoğlu G, Aydın Ş A. Evaluation of the modified mews score and charlson comorbidity index in patients with community acquired sepsis in the emergency department. *Intern Emerg Med*. Apr 2013;8(3):255–60. <https://doi.org/10.1007/s11739-012-0890-x>.
- [37] Quan H, Li B, Saunders LD, et al. Assessing validity of icd-9-cm and icd-10 administrative data in recording clinical conditions in a unique dually coded database. *Health Serv Res*. Aug 2008;43(4):1424–41.
- [38] Hainmueller J. Entropy balancing for causal effects: A multivariate reweighting method to produce balanced samples in observational studies. *Political Analysis*. 2012;20(1):25–46. <https://doi.org/10.1093/pan/mpr025>.
- [39] Chang CB, Lai HY, Hwang SJ, et al. Prescription of potentially inappropriate medication to older patients presenting to the emergency department: A nationally representative population study. *Sci Rep*. 2018;8(1):11727. <https://doi.org/10.1038/s41598-018-30184-4>.
- [40] Heider D, Matschinger H, Meid AD, et al. Health service use, costs, and adverse events associated with potentially inappropriate medication in old age in germany: Retrospective matched cohort study. *Drugs Aging*. 2017;34(4):289–301. <https://doi.org/10.1007/s40266-017-0441-2>.
- [41] Hyttinen V, Jyrkkä J, Valtonen H. A systematic review of the impact of potentially inappropriate medication on health care utilization and costs among older adults. *Med Care*. 2016;54(10):950–64. <https://doi.org/10.1097/MLR.0000000000000587>.
- [42] Jeon HL, Park J, Han E, Kim DS. Potentially inappropriate medication and hospitalization/emergency department visits among the elderly in korea. *Int J Qual Health Care*. Feb 1 2018;30(1):50–6. <https://doi.org/10.1093/intqhc/mzx171>.
- [43] Lohman MC, Cotton BP, Zagaria AB, et al. Hospitalization risk and potentially inappropriate medications among medicare home health nursing patients. *J Gen Intern Med*. 2017;32(12):1301–8. <https://doi.org/10.1007/s11606-017-4157-0>.
- [44] Marcum ZA, Handler SM, Boyce R, Gellad W, Hanlon JT. Medication misadventures in the elderly: A year in review. *Am J Geriatr Pharmacother*. Feb 2010;8(1):77–83. <https://doi.org/10.1016/j.amjopharm.2010.02.002>.
- [45] Wallace E, McDowell R, Bennett K, Fahey T, Smith SM. Impact of potentially inappropriate prescribing on adverse drug events, health related quality of life and emergency hospital attendance in older people attending general practice: A prospective cohort study. *J Gerontol A Biol Sci Med Sci*. Feb 2017;72(2):271–7. <https://doi.org/10.1093/gerona/glw140>.
- [46] Harrison L, O'Connor E, Jie C, Benzoni T, Renner CH, McCracken R. Potentially inappropriate medication prescribing in the elderly: Is the beers criteria relevant in the emergency department today? *Am J Emerg Med*. Sep 2019;37(9):1734–7. <https://doi.org/10.1016/j.ajem.2019.05.052>.
- [47] Chen YC, Hwang SJ, Lai HY, et al. Potentially inappropriate medication for emergency department visits by elderly patients in taiwan. *Pharmacoepidemiol Drug Saf*. Jan 2009;18(1):53–61. <https://doi.org/10.1002/pds.1684>.
- [48] Hu T, Dattani ND, Cox KA, et al. Effect of comorbidities and medications on frequency of primary care visits among older patients. *Can Fam Physician*. Jan 2017;63(1):45–50.
- [49] Montastruc F, Duguet C, Rousseau V, Bagheri H, Montastruc JL. Potentially inappropriate medications and adverse drug reactions in the elderly: A study in a pharmacovigilance database. *Eur J Clin Pharmacol*. 2014;70(9):1123–7. <https://doi.org/10.1007/s00228-014-1707-9>.
- [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(1):39–49. <https://doi.org/10.1007/s40266-012-0039-7>.
- [51] Budnitz DS, Shehab N, Kegler SR, Richards CL. Medication use leading to emergency department visits for adverse drug events in older adults. *Ann Int Med*. Dec 4 2007;147(11):755–65.
- [52] Gutierrez-Valencia M, Izquierdo M, Malafarina V, et al. Impact of hospitalization in an acute geriatric unit on polypharmacy and potentially inappropriate prescriptions: A retrospective study. *Geriatr Gerontol Int*. Dec 2017;17(12):2354–60. <https://doi.org/10.1111/ggi.13073>.
- [53] Hill-Taylor B, Walsh KA, Stewart S, Hayden J, Byrne S, Sketris IS. Effectiveness of the stopp/start (screening tool of older persons' potentially inappropriate prescriptions/ screening tool to alert doctors to the right treatment) criteria: Systematic review and meta-analysis of randomized controlled studies. *J Clin Pharm Ther*. Apr 2016;41(2):158–69. <https://doi.org/10.1111/jcpt.12372>.
- [54] Ishii S, Kojima T, Ezawa K, et al. The association of change in medication regimen and use of inappropriate medication based on beers criteria with adverse outcomes in japanese long-term care facilities. *Geriatr Gerontol Int*. Apr 2017;17(4):591–7. <https://doi.org/10.1111/ggi.12761>.

- [55] Ivanova I, Elseviers M, Wettermark B, Schmidt Mende K, Vander Stichele R, Christiaens T. Electronic assessment of cardiovascular potentially inappropriate medications in an administrative population database. *Basic Clin Pharmacol Toxicol*. Jan 2019;124(1):62–73. <https://doi.org/10.1111/bcpt.13095>.
- [56] Karuturi MS, Holmes HM, Lei X, et al. Potentially inappropriate medication use in older patients with breast and colorectal cancer. *Cancer*. Jul 15 2018;124(14):3000–7. <https://doi.org/10.1002/cncr.31403>.
- [57] Masumoto S, Sato M, Maeno T, Ichinohe Y, Maeno T. Potentially inappropriate medications with polypharmacy increase the risk of falls in older Japanese patients: 1-year prospective cohort study. *Geriatr Gerontol Int*. Jul 2018;18(7):1064–70. <https://doi.org/10.1111/ggi.13307>.
- [58] Perri 3rd M, Menon AM, Deshpande AD, et al. Adverse outcomes associated with inappropriate drug use in nursing homes. *Ann Pharmacother*. Mar 2005;39(3):405–11. <https://doi.org/10.1345/aph.1E230>.
- [59] Mucalo I, Hadžabić MO, Brajković A, et al. Potentially inappropriate medicines in elderly hospitalised patients according to the eu(7)-pim list, stopp version 2 criteria and comprehensive protocol. *Eur J Clin Pharmacol*. 2017;73(8):991–9. <https://doi.org/10.1007/s00228-017-2246-y>.
- [60] O'Mahony D, Gallagher P, Ryan C, et al. Stopp & start criteria: A new approach to detecting potentially inappropriate prescribing in old age. *Eur Geriatr Med*. 2010;1(1):45–51. <https://doi.org/10.1016/j.eurger.2010.01.007>.
- [61] Dalleur O, Boland B, Losseau C, et al. Reduction of potentially inappropriate medications using the stopp criteria in frail older inpatients: A randomised controlled study. *Drugs Aging*. 2014;31(4):291–8. <https://doi.org/10.1007/s40266-014-0157-5>.
- [62] Gallagher P, O'Mahony D. Stopp (screening tool of older persons' potentially inappropriate prescriptions): Application to acutely ill elderly patients and comparison with beers' criteria. *Age Ageing*. 2008;37(6):673–9. <https://doi.org/10.1093/ageing/afn197>.
- [63] Grace AR, Briggs R, Kieran RE, et al. A comparison of beers and stopp criteria in assessing potentially inappropriate medications in nursing home residents attending the emergency department. *J Am Med Dir Assoc*. 2014;15(11):830–4. <https://doi.org/10.1016/j.jamda.2014.08.008>.
- [64] Hamilton H, Gallagher P, Ryan C, Byrne S, O'Mahony D. Potentially inappropriate medications defined by stopp criteria and the risk of adverse drug events in older hospitalized patients. *Arch Intern Med*. 2011;171(11):1013–1019. doi:<https://doi.org/10.1001/archinternmed.2011.215>; 10.1038/clpt.2011.44; Barry, P.J., Gallagher, P., Ryan, C., O'Mahony, D., START (Screening Tool to Alert doctors to the Right Treatment)—an evidence-based screening tool to detect prescribing omissions in elderly patients (2007) *Age Ageing*, 36 (6), pp. 632–638
- [65] Huang CH, Umegaki H, Watanabe Y, et al. Potentially inappropriate medications according to stopp-j criteria and risks of hospitalization and mortality in elderly patients receiving home-based medical services. *PLoS ONE*. 2019;14(2):e0211947. <https://doi.org/10.1371/journal.pone.0211947>.
- [66] Sevilla-Sánchez D, Molist-Brunet N, Espauella-Panicot J, et al. Potentially inappropriate medication in palliative care patients according to stopp-frail criteria. *Eur Geriatr Med*. 2018;9(4):543–50. <https://doi.org/10.1007/s41999-018-0073-z>.
- [67] van der Stelt CA, Vermeulen Windsant-van den Tweel AM, Egberts AC, et al. The association between potentially inappropriate prescribing and medication-related hospital admissions in older patients: A nested case control study. *Drug Saf*. Jan 2016;39(1):79–87. <https://doi.org/10.1007/s40264-015-0361-1>.
- [68] Budnitz DS, Lovegrove MC, Shehab N, Richards CL. Emergency hospitalizations for adverse drug events in older Americans. *New Engl J Med*. 2011;365(21):2002–12. <https://doi.org/10.1056/NEJMsa1103053>.
- [69] Lai HY, Hwang SJ, Chen YC, Chen TJ, Lin MH, Chen LK. Prevalence of the prescribing of potentially inappropriate medications at ambulatory care visits by elderly patients covered by the taiwanese national health insurance program. *Clin ther*. Aug 2009;31(8). <https://doi.org/10.1016/j.clinthera.2009.08.023> 1859–70.
- [70] Mo L, Ding D, Pu SY, et al. Patients aged 80 years or older are encountered more potentially inappropriate medication use. *Chin Med J*. 2016;129(1):22–7. <https://doi.org/10.4103/0366-6999.172558>.
- [71] Etymologia. Bonferroni correction. *Emerg Infect Dis*. Feb 2015;21(2):289. <https://doi.org/10.3201/eid2102.et2102>.
- [72] Armstrong RA. When to use the bonferroni correction. *Ophthalmic Physiol Opt*. Sep 2014;34(5):502–8. <https://doi.org/10.1111/opo.12131>.
- [73] Curtin F, Schulz P. Multiple correlations and bonferroni's correction. *Biol Psychiatry*. Oct 15 1998;44(8):775–7. [https://doi.org/10.1016/s0006-3223\(98\)00043-2](https://doi.org/10.1016/s0006-3223(98)00043-2).