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Original Study

Over- and Underuse of Proton Pump Inhibitors in Nursing Homes: A Multisite Longitudinal Cohort Study

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A B S T R A C T

Objectives: Proton pump inhibitors (PPIs) are used to manage excess stomach acid production and provide gastroprotection from bleeding risk-increasing drugs (BRIDs). We aimed to determine the prevalence of potentially inappropriate PPI use in nursing homes and associated factors.
Design: Longitudinal cohort study using 8 years of electronic data.
Setting and Participants: The study included 6439 permanent residents aged ≥65 years from 34 homes managed by 2 aged care providers in New South Wales.
Method: Continuous PPI use (>12 weeks) in the absence of long-term BRID (>30 days) use was deemed inappropriate overuse whereas long-term BRID use without concomitant PPI for gastroprotection was classified as inappropriate underuse. Binary logistic regression was used to determine factors associated with PPI overuse.
Results: Fifty-four percent of residents (n = 3478) received a PPI, with a median duration of 46 weeks, whereas 58.5% (n = 3770) were long-term BRID users. Four of 5 PPI users (83.6%, n = 2906) used PPIs for >12 weeks, and after accounting for BRID use, the prevalence of inappropriate PPI overuse was 27.1% (n = 944). PPI overuse was 4 times more likely in residents in provider A compared with residents in provider B [odds ratio (OR) 4.08, 95% CI 2.73–6.09]. The prevalence of PPI underuse was 38.5% (n = 1452).
Conclusions and Implications: One in 4 PPI users exceeded the clinically recommended duration, whereas 2 in 5 long-term BRID users did not receive a PPI for gastroprotection. There is a pressing need for tailored interventions, such as medication reviews and deprescribing initiatives, to improve PPI prescribing.

Proton pump inhibitors (PPIs) are an important class of medicine primarily indicated for conditions associated with excessive stomach acid, such as gastroesophageal reflux disease (GERD), peptic ulcer disease, gastritis, dyspepsia, and Barrett esophagus.[1-3] They are also prescribed as a prophylaxis for gastroprotection, aiming to prevent potential adverse effects induced by medications that increase the risk of gastric irritation or bleeding, collectively known as bleeding risk–increasing drugs (BRIDs), such as nonsteroidal

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antiinflammatory drugs (NSAIDs).[4] Since their clinical introduction in 1989, the use of PPIs has dramatically increased across the world, making them one of the most prescribed medicines globally.[3,5-8] In Australia, there was a staggering 1318% increase in the use of PPIs between 1995 and 2006.[9]

PPIs are among the most common medicines dispensed particularly for older adults in Australia, with 37% of users being aged ≥65 years.[10] For instance, in 2018–2019, more than 7.1 million PPI Pharmaceutical Benefit Scheme (PBS) prescriptions were dispensed to people aged ≥75 years.[11] Use of PPIs is even more pronounced within nursing homes, also known as residential aged care or long-term facilities, where 50% or residents regularly use PPIs.[12] However, owing to their frailty and age-related changes in drug response, older adults in nursing homes are particularly susceptible to adverse effects.[13]

Although generally viewed as safe, emerging evidence underscores the potential risks associated with the overuse of PPIs. PPIs have been linked to increased susceptibility to a range of adverse events, including community-acquired pneumonia, bone fractures, vitamin B_{12} deficiencies, *Clostridium difficile* infections, and kidney damage.[7,14] In response, numerous professional and governmental organizations developed guidelines on appropriate PPI duration. The Beers Criteria, for instance, recommends limiting PPI use to less than 8 weeks, unless specific clinical circumstances necessitate longer-term administration, such as long-term BRID use.[15] The Australian Therapeutic Goods Administration (TGA) provides guidelines recommending a trial period of 4–8 weeks for GERD and dyspepsia with reassessment if symptoms persist after 8 weeks.[16,17] Additionally, the Royal Australian College of General Practitioners (RACGP) and the Gastroenterological Society of Australia (GESA) have provided recommendations within the Choosing Wisely Australia initiative.[18,19] RACGP advises against long-term PPI use in patients without complicated diseases unless attempts to reduce dosage or cease use have been made,[19] whereas GESA recommends avoiding long-term PPI prescription without attempts to lower dosage or discontinue use altogether.[18]

The rationale for this study is 2-fold. First, although there is a growing literature on PPI use in various settings, research in the context of Australian nursing homes is notably sparse.[20] The older adult population in nursing homes faces distinctive challenges such as increased risks of cognitive decline, functional limitations, polypharmacy, and concurrent use of BRIDs, underscoring the importance of investigating the nature of PPI use within this population. Second, although existing studies predominantly focus on the overuse of PPIs, there exists a significant gap in research concerning the potential underuse of PPIs across various settings globally. Numerous evidence-based guidelines highlight the importance of gastroprotection to mitigate the risk of gastric irritation and bleeding associated with prolonged BRID use.[21-24] Therefore, ensuring that long-term BRID users receive appropriate PPI prophylaxis is crucial for preventing potential adverse events and aligning resident care with established recommendations. This study aims to address this research gap by leveraging unique longitudinal medication administration data. The aim of the study is 2-fold: (1) to determine the prevalence of potentially inappropriate PPI use from both overuse and underuse perspectives in nursing homes and (2) to identify factors associated with potentially inappropriate PPI overuse in nursing homes. We hypothesize that specific resident characteristics and health conditions are associated with potentially inappropriate PPI overuse in nursing homes. In this study, the overuse of PPIs was defined as the use of PPIs for more than 12 weeks without concurrent BRID use, whereas underuse was defined as absent PPI use in long-term BRID users.

Methodology

Study design and Setting

This was a retrospective longitudinal cohort study conducted using electronic aged care data extracted from 34 nursing homes across 2 aged care providers in the Sydney metropolitan region, New South Wales, Australia. The study period was from July 1, 2014, to September 30, 2022. We selected this study period because our access to the data used in the study began in July 2014 for provider A. The data for provider B started on January 1, 2019. This study was undertaken as part of the National Aged Care Medication Roundtable, a 5-year project funded by the Australian National Health and Medical Research Council.[25] This study was reviewed and approved by the Macquarie University Human Research Ethics Committee (project ID: 11267).

Participants

The study participants were newly admitted permanent residents aged 65 years or older who entered the nursing homes on or after July 1, 2014. Residents who were already in facilities as of July 1, 2014, were excluded from the analysis because of the lack of data on their PPI use history before the study's start date. Temporary residents receiving respite or interim care were also excluded because of their short-term stays. The study participants were required to have a minimum stay of 100 days within the facility to facilitate at least 1 assessment of potentially inappropriate PPI usage, using a 12-week time frame to determine appropriateness. Our primary focus was to explore the duration and appropriateness of PPI use over time from the point of entry into the nursing homes.

Data Source

We used electronic data from aged care providers, by linking 2 databases—resident profiles and daily medication administration. The *resident profile* database contained demographic information (eg, age, gender, care provider), and baseline health conditions (eg, history of peptic ulcer/gastroesophageal disease, dementia, diabetes). The *medication administration* database included information on each medication administered to residents daily, including the medication name, dose, date and time of administration, route, and whether it was a regular or as-needed (PRN) medications. Each resident had a unique ID common to both databases that allowed linkage. We used the World Health Organization's Anatomical Therapeutic Classification (ATC) codes to identify relevant medication names and classes.

PPIs

Five PPI medicines are approved for use in Australia. In this study, we included PPIs used for acid suppression (ie, ATC A02BC) and excluded those used in combination with other medications for eradication of *Helicobacter pylori* (ie, A02BD). We identified each PPI medicine using ATC level 5 codes: omeprazole (ATC code A02BC01), pantoprazole (ATC code A02BC02), lansoprazole (ATC code A02BC03), rabeprazole (ATC code A02BC04), and esomeprazole (ATC code A02BC05). PPI medications come in varying strengths, ranging from 10 to 40 mg: 10 mg (rabeprazole, omeprazole), 15 mg (lansoprazole), 20 mg (omeprazole, rabeprazole, esomeprazole), 30 mg (lansoprazole), to 40 mg (esomeprazole, pantoprazole). In Australia, as of May 2019, only esomeprazole 40 mg was categorized as a "high-dose" PPI based on its strength, whereas other formulations are deemed standard or low-dose.[26] In the current study, the dosage of each PPI was

extracted and classified into high (for esomeprazole 40 mg), standard, or low categories for other PPI drugs and formulations.

PPIs are recommended for use as gastroprotection in individuals undergoing long-term treatment with BRIDs. Although there is not a universally agreed-on list of medications categorized as BRIDs, the long-term use of 3 medication classes are frequently referenced in the literature and have been included in our current studies: *anticoagulants* (ATC codes B01AA, B01AB, B01AD, B01AE, and B01AF), *antiplatelets* (ATC code B01AC), and *nonsteroidal anti-inflammatory drugs* (ATC codes N02BA03 and M01A, excluding glucosamine).[21]

Definition of Terminologies

The following definitions apply to all medication-related data, including PPIs and BRIDs. *Baseline users* refer to the medication usage status of residents during the initial week of their admission to the home. *Ever users* are individuals who have used a given medication at least once during their stay in the home. *Long-term users* signify individuals who have continuously used a given medication for more than 4 weeks during their stay. The concomitant PPI and BRID use was defined as the overlap in the use of these 2 medication classes for a minimum duration of 4 weeks. Polypharmacy was defined as the concurrent use of 9 or more regular medications, which is consistent with polypharmacy definitions used nationally in Australian aged care.

Each resident was tracked from entry into the facility for up to 5 years. The 5-year follow-up period was chosen as it reflects the maximum length of stay for the majority of residents in the facility. Consequently, the prevalence of PPI use was assessed throughout this time frame. The duration of PPI treatment was assessed by monitoring daily administration for each resident, allowing for a grace period of up to 7 days for any gaps. If there was a lapse exceeding 7 days in PPI administration, it was considered discontinuation. Any subsequent reinitiation of the PPIs marked the commencement of a new episode of use. In cases with multiple episodes of PPI use, we used the longest episode to determine the duration of use, including for the Kaplan-Meier curve analysis. We defined *potentially inappropriate PPI overuse* based on established guidelines and recommendations from various deprescribing algorithms.[15,27,28] Specifically, the use of PPIs for $\geq$12 weeks in residents who were not long-term BRID users (>30 days) was classified as *potentially inappropriate PPI overuse*. Although some existing literature defines inappropriateness using an 8-week time frame,[17,29,30] we opted for the 12-week threshold to provide a more conservative estimate.[5] Conversely, in cases where residents were long-term users of BRIDs but never used PPIs, we classified this as *potentially inappropriate PPI underuse*, as guidelines recommend the use of PPIs to mitigate gastrointestinal issues among long-term BRID users.[21-24]

Statistical Analysis

Descriptive statistics, including median and interquartile range (IQR), were reported as appropriate. To compare the differences in baseline characteristics between PPI users and nonusers, a Kruskal-Wallis test was used for continuous variables as our data were skewed or nonnormally distributed, whereas a χ^2 test was used for categorical variables. We used a Kaplan-Meier curve to illustrate the duration of PPI use.

To quantify the extent of exposure to each PPI during their stay, we calculated the proportion of days covered (PDC). PDC is determined by dividing the total cumulative number of days residents received a given PPI by the resident's length of stay, including fragmented days of multiple PPI exposures. This metric reflects the proportion of time residents were exposed to the PPI during their stay in nursing homes. Boxplots were used for visualizing the PDC distribution of each PPI. Pearson correlation coefficient was used to determine the correlation between the number of days PPIs were used (PPI-day) and the number of days BRIDs were used (BRID-day).

We conducted a logistic regression analysis to identify predictors of *potentially inappropriate PPI overuse* (ie, PPI use >12 weeks, yes/no) among cohorts of PPI users with non- or short-term BRID use. We specifically focused on non- or short-term BRID (<30 days) users as prolonged PPI use might be justified in residents with long-term BRID use. The predictors considered in the analysis included demographic factors (age, sex, provider), baseline health status indicators (eg, history of peptic ulcer or GERD, renal disease), number of regular medications at baseline, and year of

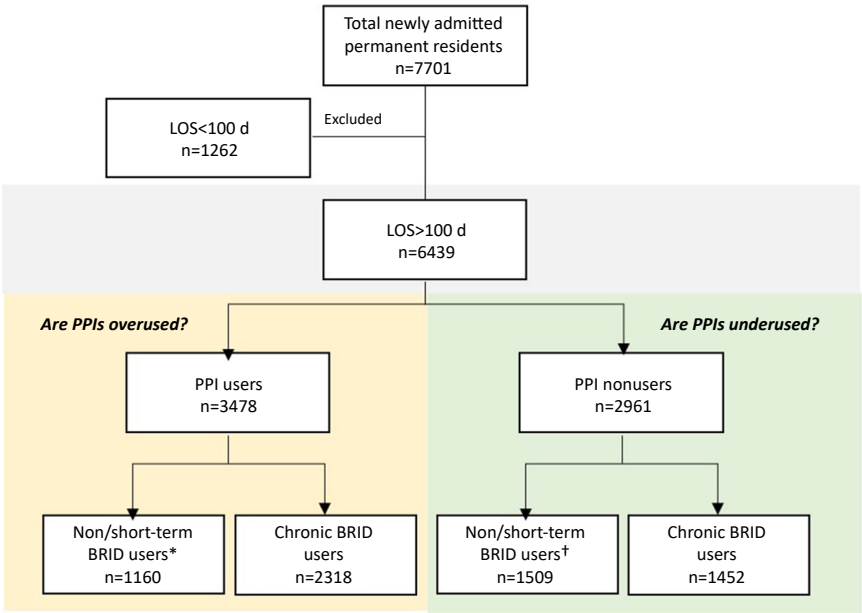

Fig. 1. Participant selection flowchart. *949 non-BRID users plus 211 short-term (<30 days) BRID users. †1295 non-BRID users plus 214 short-term BRID users. LOS, length of stay.

Table 1
Baseline Participant Characteristics by PPI Use

Variables	PPI Users (n = 3478)	PPI Non-users (n = 2961)*	Total (n = 6439)
Female	2229 (64.1)	1904 (64.3)†	4133 (64.2)
Age, y, median (IQR)	86.0 (81.0–90.0)	86.0 (80.0–90.0)†	86.0 (81.0–90.0)
Nursing home provider			
A	2727 (78.4)	2327 (78.6)	5054 (78.5)
B	751 (21.6)	634 (21.4)	1385 (21.5)
Health conditions			
Circulatory conditions, any	3200 (92.0)	2498 (84.4)	5698 (88.5)
Cerebrovascular accident	906 (26.0)	645 (21.8)	1551 (24.1)
Dementia	1539 (44.2)	1778 (60.0)	3317 (51.5)
Endocrine, any	1440 (41.4)	1015 (34.3)	2455 (38.1)
Diabetes	1042 (30.0)	694 (23.4)	1736 (27.0)
Cancer	1022 (29.4)	740 (25.0)	1762 (27.4)
Parkinson disease	183 (5.3)	178 (6.0)†	361 (5.6)
Peptic ulcer/GERD	1569 (45.1)	418 (14.1)	1987 (30.9)
Renal disease	758 (21.8)	504 (17.0)	1262 (19.6)
Arthritis	2060 (59.2)	1558 (52.6)	3618 (56.2)
History of fracture	1248 (35.9)	933 (31.5)	2181 (33.9)
Number of medicines, median (IQR)	9.0 (7.0–11.0)	6.0 (4.0–8.0)	8.0 (5.0–10.0)
Polypharmacy without PRN, n (%)	1892 (54.4)	674 (22.8)	2566 (39.9)
Medications (ATC level 1), n (%)			
Alimentary tract and metabolism	2847 (81.9)	1937 (65.4)	4784 (74.3)
Anti-infectives for systemic use	574 (16.5)	348 (11.8)	922 (14.3)
Antineoplastic and immunomodulators	125 (3.6)	89 (3.0)†	214 (3.3)
Blood and blood-forming organs	1920 (55.2)	1229 (41.5)	3149 (48.9)
Cardiovascular system	2468 (71.0)	1680 (56.7)	4148 (64.4)
Dermatologic	545 (15.7)	418 (14.1)†	
Genitourinary system and sex hormones	443 (12.7)	253 (8.5)	696 (10.8)
Musculoskeletal system	558 (16.0)	322 (10.9)	880 (13.7)
Nervous system	2504 (72.0)	1776 (60.0)	4280 (66.5)
Respiratory system	719 (20.7)	326 (11.0)	1045 (16.2)
Sensory organs	825 (23.7)	569 (19.2)	1394 (21.6)
Systemic hormonal preparations	689 (19.8)	406 (13.7)	1095 (17.0)

*The differences in the variables between the 2 groups were statistically significant at a *P* value of .05, unless otherwise indicated.
†NS, nonsignificant ($P > .05$).

admission. We assessed multicollinearity among all potential pairs of the baseline variables using correlation analysis, selecting 1 variable for further analysis when a high correlation was identified (correlation coefficient > 0.7). Subsequently, we used a forced entry method to include all relevant variables in the model to determine independent variables. The strength of association was assessed using odds ratio (OR) with a 95% CI. The analysis was conducted using Stata, version 18 (StataCorp LP, College Station, TX), and data visualization was performed using GraphPad Prism, version 10 (La Jolla, CA).

Results

Participants

The study included 6439 participants, two-thirds female (64.2%, n = 4133), with a median age of 86 years (IQR = 81.0–90.0). More than half of the residents (54.0%, n = 3478) received a PPI whereas close to three-fourths (58.5%, n = 3770) were long-term BRID users (Figure 1). Table 1 presents baseline characteristics stratified by PPI usage status. The distributions of age and sex did not exhibit significant differences based on PPI usage status. However, there were notable differences in the prevalence of several health conditions and medication use between PPI users and nonusers, with few exceptions. For instance, the proportion of residents with a history of peptic ulcer or GERD was markedly higher among PPI users compared to nonusers (45.1% vs 14.1%, $P < .001$). Conversely, the proportion of residents diagnosed with dementia was significantly higher among PPI nonusers compared with users (60.0% vs 44.2%, $P = .006$).

PPI Medicines

Pantoprazole was the most used PPI (63.6%), whereas lansoprazole was the least used PPI, with only 3.1% of residents ever using the medication. Approximately 80% (n = 2781) of PPI users used standard doses, either solely or combined with low doses during their stay. This means their maximum dose exposure fell within the standard dose range, whether through ongoing use, transitioning from low to standard dose, or vice versa. A total of 353 residents, comprising 10.1% of PPI users or 43% of esomeprazole users, used high doses at least once during the study period. The remaining residents (9.9%, n = 344) consistently used low-dose PPIs.

There was high concomitant BRID use with PPIs (72.7% of PPI users used at least 1 type of BRIDs during their stay). Antiplatelets (which includes low-dose Aspirin) was the most common BRID class (Table 2). A moderate correlation (correlation coefficient = 0.64) was observed between the number of days PPIs were used (PPI-day) and the number of days BRIDs were used (BRID-day), as depicted in Supplementary Figure 1.

Duration of PPI Use and PDC

The median number of episodes of PPI use was 2 (IQR 1–3). The overall median duration of use, considering the longest episode if residents had multiple episodes of use, was 46 weeks (IQR 19–91). Lansoprazole exhibited the shortest duration of use, with a median of 26 weeks compared with other PPIs (Figure 2A).

The median PPI PDC (ie, the proportion of days covered by any PPIs) was 81% (IQR 46–94), indicating that half of PPI users in our cohort received a PPI 4 of 5 days during their entire length of stay at the residential aged care provider. The median PDC ranged from 41.3%

Table 2
PPI Medicines and Concomitant BRID Use (n = 3478)

	Baseline, n (%)	Chronic Users, n (%)	Ever Users, n (%)
PPI			
Pantoprazole	1521 (43.7)	1997 (57.4)	2211 (63.6)
Esomeprazole	639 (18.4)	749 (21.5)	829 (23.8)
Rabeprazole	350 (10.1)	390 (11.2)	413 (11.9)
Omeprazole	242 (7.0)	302 (8.7)	336 (9.7)
Lansoprazole	53 (1.5)	89 (2.6)	107 (3.1)
Concomitant BRID			
Any BRIDs	2075 (59.7)	2318 (66.6)	2529 (72.7)
Antiplatelets	1273 (36.6)	1430 (41.1)	1528 (43.9)
Anticoagulants	841 (24.2)	994 (28.6)	1152 (33.1)
NSAIDs	102 (2.9)	222 (6.4)	546 (15.7)

(lansoprazole) to 79.4% (rabeprazole) across different PPI medicines (Figure 2B).

The median duration of PPI use was 60 weeks (IQR 29–120) for provider B compared with 42 weeks (IQR 17–83) for provider A. Supplementary Figure 2 further underscores the notable disparity between the 2 providers regarding the duration of PPI use for both residents with and without a history of peptic ulcer or GERD. For example, for residents with a history of peptic ulcer or GERD, the median duration of PPI use was 62 weeks at provider B compared with 49 weeks at provider A.

Potentially Inappropriate PPI Overuse

Four of 5 PPI users (83.6%, n = 2906) used them for a duration exceeding 12 weeks. However, among these 2906 residents, 67.5% (n = 1962) were also long-term BRID users, justifying their need for PPIs. After accounting for long-term BRID use, the prevalence of inappropriate PPI overuse was 27.1% (n = 944). In a subgroup analysis of *PPI users with no or short-term BRID use*, 81.4% (944/1160) exhibited potentially inappropriate overuse (Table 3). There was no major difference in the prevalence of inappropriate overuse when the cut point of 8 weeks was used to define appropriateness (Supplementary Table 1).

Predictors of Potentially Inappropriate PPI Overuse

Table 4 displays the results of a multivariate logistic regression model indicating predictors of inappropriate PPI overuse among cohorts of PPI users with no or short-term BRID use. Two variables (provider and history of peptic ulcer or GERD) were associated with a higher likelihood of experiencing inappropriate overuse, whereas 2 variables (endocrine disease and renal disease) were associated with a lower likelihood.

Importantly, residents in facilities managed by provider B were approximately 4 times more likely to experience inappropriate PPI overuse compared with residents in facilities managed by provider A (OR 4.08, 95% CI 2.73–6.09). Residents with a history of peptic ulcer or GERD were 2.45 times more likely to experience inappropriate PPI overuse compared with their counterparts (OR 2.45, 95% CI 1.87–3.22).

Potentially Inappropriate PPI Underuse

As illustrated in Figure 1, two-thirds (66.6%, n = 2318) of PPI users were also long-term BRID users, whereas half (49.0%, n = 1452) of the PPI nonusers were long-term BRID users. This indicates that 22.5% (n = 1452) of the total sample (n = 6439) or 38.5% of long-term BRID users (n = 3770) did not receive any PPIs during the follow-up period despite using BRIDs on a long-term basis. This represents a potential underuse of PPIs. Additional data on BRID use among PPI users and nonusers are presented in Supplementary Table 2.

Supplementary Figure 3 compares the PDC values of each BRID class among long-term users (>30 days of use), showing a higher PDC value for each BRID class among PPI nonusers compared with PPI users except for NSAIDs. For instance, in long-term anticoagulant users, the median PDC value for anticoagulants was greater in PPI nonusers compared with users (86.4% vs 79.8%, $P < .001$). This suggests that anticoagulants were used for 86.4% of their stay in the facilities without concurrent PPI use.

Discussion

Summary

This multisite longitudinal cohort study investigated the use and appropriateness of PPIs for both overuse and potential underuse. The study found that 54% of residents received a PPI with a median duration of 46 weeks. Our study used stringent criteria to assess the appropriateness of PPI overuse, using a 12-week cutoff and considering the prophylactic use of PPIs for long-term BRID use (NSAIDs, antiplatelets, and anticoagulants) as justifiable regardless of their duration. We found that when disregarding prophylactic use, 83.6% of PPI users had used them for longer than 12 weeks. However, when accounting for prophylactic use, the prevalence significantly dropped to 27%. This finding emphasizes the importance of contextualizing PPI use within the broader scope of a resident's medication regimen. We identified a significant provider-level discrepancy, with provider B exhibiting a 4-fold higher likelihood of potentially inappropriate PPI overuse compared with provider A. One in 5 residents overall, or 2 in 5 long-term BRID users, did not receive prophylactic PPI for gastroprotection, contradicting evidence-based recommendations.[21-24]

Comparison With Existing Literature

Comparison of our findings with existing literature must be approached with caution. Direct comparisons may be misleading because of significant differences in study designs, criteria used to assess appropriateness, the thoroughness of medication reviews addressing inappropriate use, and health care practices across different settings. First, our estimate of the prevalence of potentially inappropriate PPI overuse is based on treatment durations informed by evidence-based guidelines.[15,27,28] In addition to treatment duration, existing research uses diverse methodologies, including indication-based assessments, expert opinions (eg, gastroenterologists assessment), and criteria such as the Beers Criteria, STOPP (Screening Tool of Older Persons' Prescriptions), and the FORTA (Fit fOR The Aged) list.[31] Second, differences also emerge regarding the consideration of BRIDs: some studies overlook concurrent BRID use when assessing PPI appropriateness, some focus on NSAIDs and antiplatelets (mainly Aspirin) whereas others considered NSAIDs, antiplatelets, and anticoagulants (eg, warfarin).[32-35] Third, for studies using treatment duration, the choice of cutoff to define appropriateness (eg, 8 weeks vs 12 weeks) may also account for discrepancies, although in our study, no significant differences were noted (27% with 12 weeks compared to 28% with 8 weeks). These variabilities underscore the necessity for a standardized approach to determine appropriateness, facilitating clearer insights and harmonizing future research efforts.

Existing studies reported wide variability in the rates of inappropriate PPI use in nursing homes, ranging from 12% to 63%,[20,34-41] highlighting the inconsistency in prescribing practices across different settings and geographical locations. A small Australian study (n = 383) from 6 nursing homes defined inappropriate use as PPI use for >8 weeks without documented indications or prophylaxis for concomitant BRIDs and reported a low rate of inappropriate PPI use at

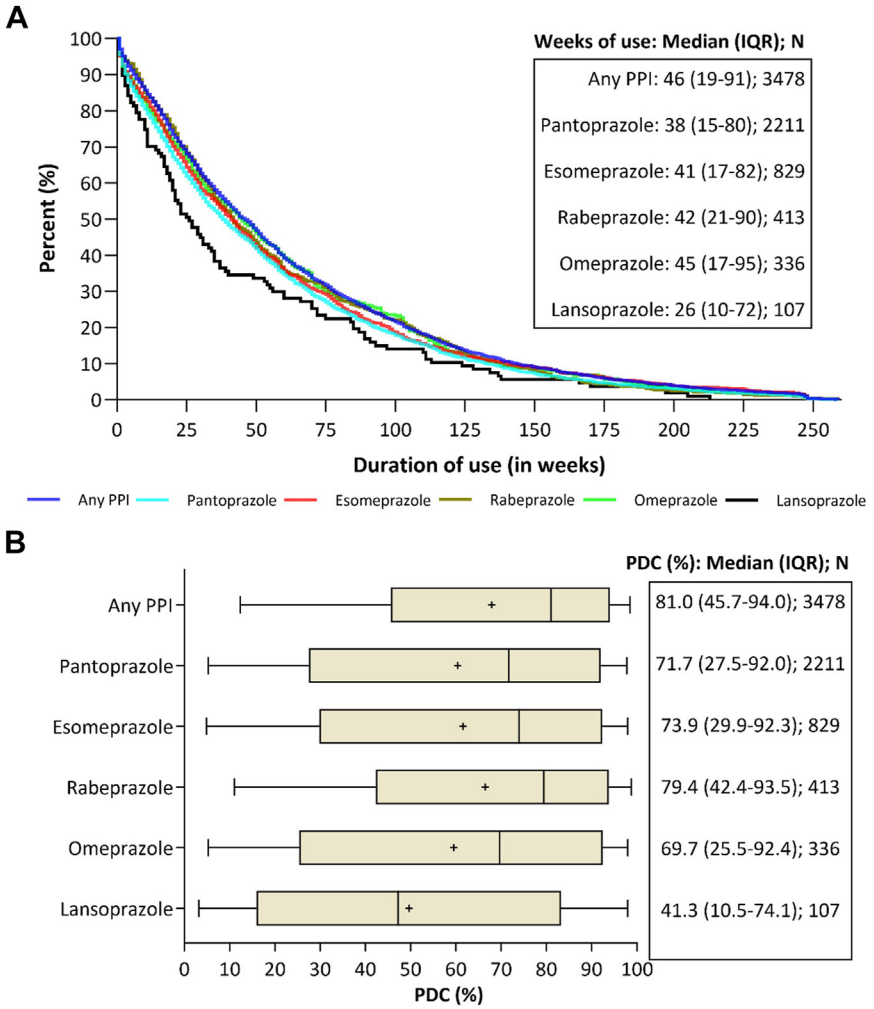

Fig. 2. (A) Kaplan-Meier survival curve showing the duration of use of each PPI, and (B) box plots showing the PDC values for each PPI. Boxes represent the IQR with the median value within the boxes, the mean value is represented as a "+" and the capped bars represent the 10th and 90th percentiles.

12%.[20] Facilities in that study may have achieved greater adherence to prescribing guidelines or more rigorous medication review processes than our study sites. In contrast, a large-scale US study involving 13.5 million nursing home residents reported that 49% of PPI use was not evidence-based according to the US Food and Drug Administration (FDA) and National Institute for Health and Care Excellence (NICE) guidelines.[36] This study considered the use of PPIs for cotherapy for NSAIDs as justifiable but did not account for antiplatelets and anticoagulants, unlike our study. Another US study involving 1381 residents from 22 nursing homes reported a 65% prevalence of inappropriate PPI use when disregarding prophylactic use of PPIs for BRIDs.[35] This figure dropped to 24% after considering the prophylactic use of PPIs for NSAIDs, aspirin (antiplatelet), and anticoagulants as appropriate, demonstrating the significant impact of accounting for these medications in this vulnerable population. An Italian study by Pasina et al, which included 2579 residents from 27 nursing homes, reported that nearly half of PPI users were using the medication inappropriately, with facility-level rates ranging from 22% to 63%.[37] This wide range within a single country underscores the disparities in local prescribing practices and implementation of clinical guidelines. Other international studies corroborate the widespread issue of inappropriate PPI use in nursing homes: a Spanish study found a 12% rate, whereas studies in Taiwan, Portugal, Ireland, and Canada reported rates of 27%, 58%, 59%, and 63%, respectively.[34,38-41]

Table 3
Proportion of Residents Experiencing Potentially Inappropriate PPI Overuse Using a 12-Week Cutoff to Define Appropriateness

Cutoff	Regardless of BRID Use (n = 3478)	Inappropriate Overuse	
		Accounting for Long-term BRID Use* (n = 3478)	Nonusers or Short-Term BRID Users Only (n = 1160)
>12 wk	2906 (83.6)	944 (27.1)	944 (81.4)

*Long-term BRID users were excluded from the numerator (ie, not assessed for appropriateness regardless of the duration of PPI use).

In our cohort, the aged care provider emerged as a significant determinant of PPI overuse. We hypothesize that this disparity could be attributed to differences in the implementation of national quality improvement programs, such as the Quality Use of Medicines (QUM) and Residential Medication Management Review (RMMR) programs, variations in internal quality improvement initiatives, or unique deprescribing barriers faced by each provider. These barriers might include prescriber and staff knowledge gaps, and challenges related to obtaining resident or family consent.[20,42] Additionally, poor PPI administration practices within a facility may render PPIs ineffective, leading to persistent symptoms and continued prescriptions.[11]

Table 4
Multivariate Binary Logistic Model Showing Baseline Factors Associated With PPI Overuse Among PPI Users With No or Short-Term BRID Use (n = 1160)

Variable	OR	95% CI		*P*
		Lower	Upper	
Female vs male	1.10	0.79	1.52	.59
Age, y	1.01	0.99	1.03	.33
Provider B vs A	4.20	2.69	6.58	<.001
History of peptic ulcer or GERD	2.45	1.87	3.22	<.001
Cardiovascular disease	1.36	0.93	2.00	.11
Disease of central nervous systems	1.08	0.65	1.82	.76
Musculoskeletal disease	1.09	0.82	1.45	.55
Cancer	0.94	0.68	1.29	.69
Respiratory disease	1.04	0.69	1.57	.86
Endocrine disease	0.68	0.48	0.98	.036
Renal disease	0.64	0.46	0.90	.010
Number of regular medicines at baseline	1.04	0.98	1.10	.21
Year of admission	0.96	0.91	1.02	.19

Doctors working within different aged care providers may also prescribe PPIs for longer than clinically indicated because of a lack of awareness about clinical guidelines. Research indicate that many prescribers are either unaware of PPI guidelines or are hesitant to wean patients off PPIs because of concerns about symptom relapse, either their own or those of the patient and their family.[11] However, further mixed-method research is needed to confirm the causes of variation in PPI overuse between aged care providers and to inform targeted deprescribing interventions.

Policy and Practice Implications

Our study shows that despite nationwide guidelines and campaigns such as NPS MedicineWise and Choosing Wisely, significant discrepancies persist between guideline recommendations and the actual use of PPIs in nursing homes.[43] Our study findings highlight the critical need for optimizing PPI therapy, addressing both overuse and underuse of PPIs to enhance care for older adults in residential aged care facilities. In light of the significant heterogeneity in PPI use both within Australia and globally, we propose developing a standardized framework that integrates existing guidelines and protocols specifically for nursing homes. This framework should consolidate best practices from current medication management strategies, focusing on regular medication reviews, clear documentation of PPI indications, and established protocols for prophylaxis in patients with concomitant BRIDs. Additionally, comprehensive training programs for health care providers will enhance their understanding of appropriate PPI prescribing and foster adherence to these integrated guidelines. By creating a cohesive approach to medication management, we can reduce variability in PPI use and improve patient outcomes across diverse nursing home settings.

Our findings show that more than a quarter of PPI users (27%) in nursing homes could benefit from deprescribing. Deprescribing is a complex, multistep process that requires a coordinated effort among stakeholders, including health care providers, patients, and caregivers.[44] The study thus marks the initial step of identifying "potential" cases for deprescribing. The next step involves gaining a deeper understanding of the clinical context of these residents, which can be achieved through thorough medication management reviews. In Australia, government-funded programs such as the RMMR and the on-site pharmacist program are available to improve medication use in nursing homes.[45,46] These residents should be prioritized for participation in such programs. The RMMR program offers comprehensive medication review services, which aim to optimize medication use and minimize adverse drug events.[45] It is also crucial to gauge the residents' willingness and readiness to deprescribe.[47]

Our study revealed that 2 in 5 long-term BRID users may be missing out on the potential prophylactic benefits of PPIs because of underprescribing. Although addressing medication overuse has traditionally been the main focus in aged care settings, underuse is an equally important concern that has received less attention.[48] BRIDs are associated with an increased risk of gastrointestinal bleeding and other complications, making appropriate PPI use essential for mitigating these risks.[21-24] Therefore, a balanced approach that considers both over- and underuse of PPIs is crucial for improving medication management and overall health outcomes in this vulnerable population.

Our study has also health system implications. The substantial provider-level difference in the prevalence of potentially inappropriate PPI overuse emphasizes the pressing need for a more robust data infrastructure within the aged care sector. This infrastructure must be capable of facilitating comparisons and benchmarks, thereby empowering nursing homes to attain clear insights into prescribing practices within their facilities. Despite Australia's introduction of mandatory reporting, which includes 2 medication indicators—polypharmacy and antipsychotics—this initiative falls short in accounting for case-mix and local contextual factors.[49] Expanding data infrastructure would not only allow nursing homes to identify areas for improvement internally but also foster collaboration and shared learning across the sector.[25] This broader approach holds the potential to drive systemic improvements in medication management practices and resident care standards.

Strength and Limitations

Our study had several strengths, including a large sample of nearly 6500 participants from 34 facilities spanning 2 providers, adding to its robustness and generalizability. Our longitudinal design used 8 years of data, with each resident followed for up to 5 years, ensuring a thorough understanding of medication trends over time. The study also leveraged unique medication administration data rather than relying on medication claims, prescription, or dispensing records. This provided more accurate documentation of the medications received by each resident and enabled a granular analysis of PPI usage on a daily basis (eg, PDC by each PPI). Finally, to our knowledge, this study is the first to shed light on potential PPI underprescribing practices in nursing home settings. However, our study has some limitations. The assessment of appropriateness was solely based on treatment duration, without considering individual resident contexts, such as acute or evolving medical conditions that may necessitate the use of PPIs, because of the absence of such data. Our definition of underuse was based on the absence of PPI use in residents receiving BRIDs and did not include instances where the duration of PPI use was below the recommended 8 or 12 weeks, although this may also suggest underuse. Although we appropriately excluded long-term users of BRIDs from being assessed as inappropriate, regardless of their duration of PPI use, we were unable to extend this consideration to certain other medical conditions (eg, Barrett esophagus, Zollinger-Ellison syndrome, severe erosive esophagitis) that should have also been exempted,[17] because of the lack of data availability on these conditions. The health conditions data, including information on gastric bleeding, is limited to the baseline. As a result, we were unable to examine the relationship between the underuse or overuse of medications and the incidence of gastric bleeding during the follow-up period. Future research should focus on incorporating longitudinal data to gain a clearer understanding of these associations. These limitations underscore an inherent challenge when relying on routinely

collected data for research purposes, as not all relevant information may be readily available for analysis.

Conclusions and Implications

Our study revealed notable quality and safety issues regarding the use of PPIs in nursing homes, related to both overuse and underuse. One in 4 PPI users exceeded the recommended duration outlined in clinical guidelines, whereas 2 in 5 long-term BRID users were not prescribed PPIs for gastroprotection, potentially depriving them of the prophylactic benefits. These results underscore the necessity for tailored interventions, such as medication reviews and deprescribing initiatives, to reduce inappropriate PPI usage.

Disclosure

The authors declare no conflicts of interest.

Supplementary Data

Supplementary data related to this article can be found online at https://doi.org/10.1016/j.jamda.2024.105393.

References

1. Boparai V, Rajagopalan J, Triadafilopoulos G. Guide to the use of proton pump inhibitors in adult patients. *Drugs*. 2008;68:925–947.
2. Savarino V, Di Mario F, Scarpignato C. Proton pump inhibitors in GORD an overview of their pharmacology, efficacy and safety. *Pharm Res*. 2009;59:135–153.
3. Jaynes M, Kumar AB. The risks of long-term use of proton pump inhibitors: a critical review. *Ther Adv Drug Saf*. 2019;10:2042098618809927.
4. Gwee KA, Goh V, Lima G, Setia S. Coprescribing proton-pump inhibitors with nonsteroidal anti-inflammatory drugs: risks versus benefits. *J Pain Res*. 2018;11:361–374.
5. Daniels B, Pearson SA, Buckley NA, Bruno C, Zoega H. Long-term use of proton-pump inhibitors: whole-of-population patterns in Australia 2013-2016. *Therap Adv Gastroenterol*. 2020;13:1756284820913743.
6. Strand DS, Kim D, Peura DA. 25 years of proton pump inhibitors: a comprehensive review. *Gut Liver*. 2017;11:27–37.
7. Maes ML, Fixen DR, Linnebur SA. Adverse effects of proton-pump inhibitor use in older adults: a review of the evidence. *Ther Adv Drug Saf*. 2017;8:273–297.
8. Ngwenya S, Simin J, Brusselaers N. Maintenance proton pump inhibitor use associated with increased all-cause and cause-specific mortality in Sweden. *Dig Dis Sci*. 2023;68:2252–2263.
9. Hollingworth S, Duncan EL, Martin JH. Marked increase in proton pump inhibitors use in Australia. *Pharmacoepidemiol Drug Saf*. 2010;19:1019–1024.
10. Shanika LGT, Reynolds A, Pattison S, Braund R. Proton pump inhibitor use: systematic review of global trends and practices. *Eur J Clin Pharmacol*. 2023;79:1159–1172.
11. Care ACoSaQiH. Proton pump inhibitor medicines dispensing, 75 years and over. The Fourth Australian Atlas of healthcare variation. Australian Commission on safety and quality in health care. Accessed March 18, 2024. https://www.safetyandquality.gov.au/sites/default/files/2021-04/fourth_atlas_2021_-_6.3_ppi_medicines_dispensing_75_years_and_over.pdf
12. Fick DM, Semla TP, Beizer J, et al. American Geriatrics Society 2015 updated Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2015;63:2227–2246.
13. Alruthea S, Bowman P, Tariq A, Hinchcliff R. Interventions to enhance medication safety in residential aged-care settings: an umbrella review. *Br J Clin Pharmacol*. 2022;88:1630–1643.
14. Haastrup PF, Thompson W, Søndergaard J, Jarbøl DE. Side effects of long-term proton pump inhibitor use: a review. *Basic Clin Pharmacol Toxicol*. 2018;123:114–121.
15. By the American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2023;71:2052–2081.
16. Targownik LE, Fisher DA, Saini SD. AGA clinical practice update on deprescribing of proton pump inhibitors: expert review. *Gastroenter*. 2022;162:1334–1342.
17. Turner J, Thompson W, Reeve E, Bell J. Deprescribing proton pump inhibitors. *Aust J Gen Pract*. 2022;51:845–848.
18. Choosing Wisely Australia. Do not repeat colonoscopies more often than recommended by the National Health and Medical Research Council (NHMRC) endorsed guidelines. 2024. Accessed April 4, 2024. https://www.choosingwisely.org.au/recommendations/gesa
19. Choosing Wisely Australia. Recommendations the Royal Australian College of general Practitioners. 2023. Accessed November 1, 2023. https://www.choosingwisely.org.au/recommendations/racgp1
20. Hendrix I, Page AT, Korhonen MJ, et al. Patterns of high-dose and long-term proton pump inhibitor use: a cross-sectional study in six south Australian residential aged care services. *Drugs Real World Outcomes*. 2019;6:105–113.
21. Kanno T, Moayyedi P. Who needs gastroprotection in 2020? *Curr Treat Options Gastroenterol*. 2020;18(4):557–573.
22. Abrignani MG, Lombardo A, Braschi A, Renda N, Abrignani V. Proton pump inhibitors and gastroprotection in patients treated with antithrombotic drugs: a cardiologic point of view. *World J Cardiol*. 2023;15:375–394.
23. Freedberg DE, Kim LS, Yang Y-X. The risks and benefits of long-term use of proton pump inhibitors: expert review and best practice advice from the American Gastroenterological Association. *Gastroenterology*. 2017;152:706–715.
24. Lanza FL, Chan FKL, Quigley EMM, Practice Parameters Committee of the American College of G. Guidelines for prevention of NSAID-related ulcer complications. *Am J Gastroenterol*. 2009;104:728.
25. Westbrook JI, Seaman K, Wabe N, et al. Designing an informatics infrastructure for a national aged care medication roundtable. *Stud Health Technol Inform*. 2024;310:404–408.
26. NPS Medicinewise. Proton pump inhibitors: PBS changes May 2019. 2024. Accessed November 1, 2023. https://www.nps.org.au/radar/articles/proton-pump-inhibitors-pbs-changes-may-2019
27. NSW Therapeutic Advisory Group. Deprescribing guide for proton pump inhibitors (PPIs). 2024. Accessed November 1, 2023. https://www.nswtag.org.au/wp-content/uploads/2018/06/1.9-Deprescribing-Guide-for-Proton-Pump-Inhibitors-PPIs.pdf
28. Farrell B, Pottie K, Thompson W, et al. Deprescribing proton pump inhibitors: evidence-based clinical practice guideline. *Can Fam Physician*. 2017;63:354–364.
29. Giannini EG, Crespi M, Djahandideh A, et al. Appropriateness of proton pump inhibitors treatment in clinical practice: prospective evaluation in outpatients and perspective assessment of drug optimisation. *Dig Liver Dis*. 2020;52:862–868.
30. Liu Y, Zhu X, Li R, Zhang J, Zhang F. Proton pump inhibitor utilisation and potentially inappropriate prescribing analysis: insights from a single-centred retrospective study. *BMJ Open*. 2020;10:e040473.
31. Wilsdon TD, Hendrix I, Thynne TR, Mangoni AA. Effectiveness of interventions to deprescribe inappropriate proton pump inhibitors in older adults. *Drugs Aging*. 2017;34:265–287.
32. Voukelatou P, Vrettos I, Emmanouilidou G, et al. Predictors of inappropriate proton pump inhibitors use in elderly patients. *Curr Geront Ger Res*. 2019;2019:7591045.
33. Koggel LM, Lantinga MA, Büchner FL, et al. Predictors for inappropriate proton pump inhibitor use: observational study in primary care. *Br J Gen Pract*. 2022;72:e899.
34. Doell A, Walus A, To J, Bell A. Quantifying candidacy for deprescribing of proton pump inhibitors among long-term care residents. *Can J Hosp Pharm*. 2018;71:302–307.
35. Patterson Burdsall D, Flores HC, Krueger J, et al. Use of proton pump inhibitors with lack of diagnostic indications in 22 midwestern US skilled nursing facilities. *J Am Med Dir Assoc*. 2013;14:429–432.
36. Rane PP, Guha S, Chatterjee S, Aparasu RR. Prevalence and predictors of non-evidence based proton pump inhibitor use among elderly nursing home residents in the US. *Res Social Adm Pharm*. 2017;13:358–363.
37. Pasina L, Novella A, Elli C, Nobili A, Ianes A. Overuse of proton pump inhibitors in nursing homes: an Italian multicenter observational study. *Pharmacoepidemiol Drug Saf*. 2020;29:461–466.
38. Díez R, Cadenas R, Susperregui J, et al. Potentially inappropriate medication and polypharmacy in nursing home residents: a cross-sectional study. *J Clin Med*. 2022;11:3808.
39. Chang BC-C, Tsou M-T, Wu S-C. Impact of potentially inappropriate medications on unplanned hospitalization among nursing home residents: a retrospective cohort study. *Int J Gerontol*. 2022;16.
40. Plácido AI, Aguiar A, Piñeiro-Lamas M, et al. Assessment of potentially inappropriate medications using the EU (7)-PIM list, in a sample of Portuguese older adults' residents in nursing homes. *Risk Manag Healthc Policy*. 2022;15:1343–1352.
41. Kennedy C, Ow G, Bourke R, Fallon M, Fitzpatrick F, Martin A. 078A study of the prevalence and appropriateness of proton pump inhibitor prescriptions in an Irish nursing home cohort. *Age Ageing*. 2017;46(Suppl_3):iii13–iii59.
42. Swed S, Alibrahim H, Bohsas H, et al. Evaluating physicians' awareness and prescribing trends regarding proton pump inhibitors: a cross-sectional study. Original research. *Front Pharmacol*. 2023;14.
43. Bruno C, Pearson SA, Daniels B, Buckley NA, Schaffer A, Zoega H. Passing the acid test? Evaluating the impact of national education initiatives to reduce proton pump inhibitor use in Australia. *BMJ Qual Saf*. 2020;29:365–373.
44. Scott IA, Hilmer SN, Reeve E, et al. Reducing inappropriate polypharmacy: the process of deprescribing. *JAMA Intern Med*. 2015;175:827–834.
45. Pharmaceutical Society of Australia. Guidelines for pharmacists providing residential medication management review (RMMR) and quality use of medicines (QUM) services. 2024. Accessed September 23, 2024. https://my.psa.org.au/servlet/fileField?entityId=ka17F000000cmjcQAA&field=PDF_File_Member_Content__Body__s

46. Department of Health and Aged Care. Aged care on-site pharmacists consultation paper. Accessed November 1, 2023. https://consultations.health.gov.au/aged-care-division/aged-care-on-site-pharmacists
47. Chock YL, Wee YL, Gan SL, Teoh KW, Ng KY, Lee SWH. How willing are patients or their caregivers to deprescribe: a systematic review and meta-analysis. *J Gen Intern Med*. 2021;36:3830–3840.
48. Pharmaceutical Society of Australia. Medicine safety: aged care. 2023. Accessed September 23, 2024. https://www.psa.org.au/advocacy/working-for-our-profession/medicine-safety/aged-care
49. Australian Government Department of Health and Aged Care. National aged care mandatory quality indicator (QI) program. Accessed November 1, 2023. https://www.health.gov.au/our-work/qi-program