Received: 2 August 2022 | Revised: 12 February 2023 | Accepted: 15 February 2023

DOI: 10.1111/bcp.15727

ORIGINAL ARTICLE

Towards Optimizing Hospitalized Older adults' MEdications (TO HOME): Multi-centre study of medication use and outcomes in routine care

Sarah N. Hilmer[1] | Sarita Lo[1] | Patrick J. Kelly[2] | Rosalie Viney[3] | Fiona M. Blyth[2] | David G. Le Couteur[4] | Andrew J. McLachlan[5] | Sheena Arora[3] | Lutfun Hossain[3] | Danijela Gnjidic[5]

[1]Kolling Institute, The University of Sydney and Royal North Shore Hospital, St Leonards, Australia

[2]Sydney School of Public Health, Faculty of Medicine and Health, The University of Sydney, Sydney, New South Wales, Australia

[3]Centre for Health Economics Research and Evaluation, University of Technology, Sydney, Australia

[4]Centre for Education and Research on Ageing, Concord Hospital and The University of Sydney, Concord, Australia

[5]Sydney Pharmacy School, Faculty of Medicine and Health, The University of Sydney, Sydney, Australia

Correspondence
Sarah N. Hilmer, Kolling Institute, The University of Sydney and Royal North Shore Hospital, St Leonards, Australia.
Email: sarah.hilmer@sydney.edu.au

Funding information
This research was funded by NSW Health Translational Research Grant 274; Northern Sydney Local Health District; Sydney Local Health District; and Penney Ageing Research Unit, Royal North Shore Hospital, NSW, Australia.

Aims: Comprehensively investigate prescribing in usual care of hospitalized older people with respect to polypharmacy; potentially inappropriate medications (PIMs) according to Beers criteria; and cumulative anticholinergic and sedative medication exposure calculated with Drug Burden Index (DBI). Specifically, to quantify exposure to these measures on admission, changes between admission and discharge, associations with adverse outcomes and medication costs.

Methods: Established new retrospective inpatient cohort of 2000 adults aged ≥75 years, consecutively admitted to 6 hospitals in Sydney, Australia, with detailed information on medications, clinical characteristics and outcomes. Conducted cross-sectional analyses of index admission data from cohort.

Results: Cohort had mean (standard deviation) age 86.0 (5.8) years, 59% female, 21% from residential aged care. On admission, prevalence of polypharmacy was 77%, PIMs 34% and DBI > 0 in 53%. From admission to discharge, mean difference (95% confidence interval) in total number of medications increased 1.05 (0.92, 1.18); while prevalence of exposure to PIMs (−3.8% [−5.4, −2.1]) and mean DBI score (−0.02 [−0.04, −0.01]) decreased. PIMs and DBI score were associated with increased risks (adjusted odds ratio [95% confidence interval]) of falls (PIMs 1.63 [1.28, 2.08]; DBI score 1.21[1.00, 1.46]) and delirium (PIMs 1.76 [1.38, 1.46]; DBI score 1.42 [1.19, 1.71]). Each measure was associated with increased risk of adverse drug reactions (polypharmacy 1.42 [1.19, 1.71]; PIMs 1.87 [1.40, 2.49]; DBI score 1.90 [1.55, 2.15]). Cost (AU$/patient/hospital day) of medications contributing to PIMs and DBI was low ($0.29 and $0.88).

Conclusion: In this large cohort of older inpatients, usual hospital care results in an increase in number of medications and small reductions in PIMs and DBI, with variable associations with adverse outcomes.

KEYWORDS
deprescribing, Drug Burden Index, elderly, hospital, polypharmacy, potentially inappropriate medications

1 | INTRODUCTION

Optimal healthcare for older people involves using medications to address what matters to the older person and to minimize the adverse effects of medications on the person's mobility and mentation.[1] Older people admitted to hospital have a high prevalence of high-risk prescribing including polypharmacy (multiple medicine use)[2] and adverse drug events.[3] Medication use may be a modifiable contributing factor for important common adverse outcomes in older inpatients such as falls, delirium and pressure areas.[4] During a hospital stay, patients frequently receive new diagnoses and treatments. These may affect overall prognosis and may directly result in drug–drug or drug–disease interactions, which can impact on appropriateness, safety and effectiveness of existing treatments.[5] Therefore, a hospital stay is an opportunity to review and intervene to optimize medication use in older people.

The extent of high-risk prescribing in usual care, how it is addressed, its clinical associations and costs are difficult to assess. Most large-scale studies using routine data lack detail, particularly accurate information on prescribing changes in hospital and measures of geriatric outcomes.[6] In-depth medical record reviews are usually conducted at a small scale and unlikely to be representative or generalizable.[7]

We conducted a real-world, retrospective multicentre cohort study of high-risk prescribing in older inpatients. We established a new inpatient cohort of 2000 older adults, consecutively admitted to 6 hospitals of different sizes in different regions of metropolitan Sydney, Australia. The aim of this study is to investigate medications prescribed in the usual care of hospitalized older people with respect to 3 measures of high-risk prescribing: polypharmacy, potentially inappropriate medications (PIMs) according to Beers criteria and the Drug Burden Index (DBI). Specifically, this study investigates prevalence of these measures on admission, changes between admission and discharge, associations of these measures with adverse outcomes in hospital and the costs of medications contributing to PIMs and DBI.

What is already known about this subject

- Polypharmacy and medication-related harm are common in older people admitted to hospital.
- Medication review is recommended for older people in hospital.
- The extent, management, outcomes and costs of medication use in older people in routine hospital care have not been comprehensively assessed.

What this study adds

- A new multisite retrospective cohort of 2000 consecutive inpatients aged ≥75 with in-depth clinical and drug data.
- Observed high prevalence of polypharmacy, potentially inappropriate medications (PIMs) and Drug Burden Index (DBI > 0).
- With usual hospital care, total number of medications taken increased, with small decreases in PIMs and DBI.
- Polypharmacy, PIMs and DBI were all associated with an increased risk of adverse drug reactions.

2 | METHODS

2.1 | Study design and population

A retrospective multicentre cohort study of 2000 individuals aged ≥75 years and admitted to 6 metropolitan hospitals in Sydney, New South Wales, Australia. Six hospital sites of varying sizes within 2 local health districts were chosen to ensure a representative, real-world, generalizable sample within the limitations of feasible data collection for the proposed study timeframe and budget. A stratified consecutive sampling strategy was used to assemble the cohort and guide data collection.

Data on medication use and clinical outcomes were collected for patients who met the following inclusion criteria: (a) aged ≥75 years; (b) consecutively admitted to Royal North Shore ($n = 600$), Ryde ($n = 200$), Hornsby Ku-ring-gai ($n = 200$), Concord Repatriation General ($n = 700$), Canterbury ($n = 200$) and Balmain ($n = 100$) hospitals, from 1 July 2016 for >48 h, under the care of general medicine, geriatric medicine and/or rehabilitation services. Patients who did not survive the hospital stay were excluded. The latest date of hospital admission for the cohort was 31 May 2017, and the latest discharge date was 21 June 2017.

Ethics approval, with a waiver of consent, was obtained from the NSW Population and Health Services Research Ethics Committee (HREC/17/CIPHS/30). All data were de-identified prior to analysis.

2.2 | Data collection

Individuals who met study inclusion and exclusion criteria were electronically identified by the Performance Unit at each Local Health District. Potential duplication within and between the Local Health

Districts was managed through buffering the data extract to an additional 20% and then manual screening to ensure a cohort of 2000 unique individuals. Sociodemographic, clinical characteristics, diagnoses and clinical outcomes in hospital data, described in the data extracts from the Performance Units, were verified in the electronic medical record (eMR) system (Cerner Millennium PowerChart) and then manually entered into a specially built REDCap study database, a secure web application designed for online capture of research data (REDCap Software—Version 9.2.5 © 2019 Vanderbilt University, Sydney Local Health District installation). All data were collected by trained clinical researchers.

An inter-rater check was completed for a random sample of 15% of the study population on demographic data (date of birth, admission and discharge dates, allergy status, residential setting prior to hospital admission, discharge status, dementia/mild cognitive impairment status), clinical outcome data (falls, pressure areas and delirium) and medication data (medication use at admission and discharge, and the types of medication-related interventions [e.g. dose modification or cessation] made during the hospital stay; $n = 300$).

Residential setting prior to hospital admission included home, residential aged care facility and assisted living. Discharge destination included home, residential aged care facility and assisted living, public or private hospital, respite, and hospice.

Primary reason for admission, diagnoses throughout the hospital stay and clinical outcomes data, obtained from the Performance Unit, were coded using International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) coding. This is an alphanumeric coding scheme for diseases and external causes of injury, adapted from the World Health Organization (WHO) ICD-10 codes for use in Australian clinical practice. The ICD-10-AM codes were used to calculate Charlson Comorbidity Index following published guidance.[8] The use of ICD-10-AM codes to score Charlson Comorbidity Index was validated against 300 individuals in whom the Charlson Comorbidity Index was manually scored from the eMR.

2.3 | Definition of dementia and mild cognitive impairment

Dementia status was established based on whether a diagnosis was recorded in the eMR, including admission notes, inpatient clinical notes and discharge summary generated during the hospital stay. Similarly, mild cognitive impairment was defined as explicit documentation of a diagnosis in the eMR. For the index hospital stay, each patient was classified as having either dementia or mild cognitive impairment, not both.

2.4 | Definition of clinical outcomes

A fall was defined as any unintended event that results in a person coming to rest on the ground/floor/other lower-level falls (as a presenting complaint or occurred during the hospital stay). A pressure area was defined as any area of damage to the skin and underlying tissues caused by constant pressure or friction (as a presenting complaint or occurred during the hospital stay). Delirium was defined as a sudden state of severe confusion and rapid changes in brain function (previous history, presenting complaint or developed during the hospital stay).

A suspected adverse drug reaction (ADR) was defined as any injury resulting from a medical intervention related to a drug. ICD10-AM codes from data extracts were used to detect ADRs using a previously externally validated method.[9] ICD-10 external cause codes Y40–Y59 were used to ascertain ADR events caused by a medicine properly administered at therapeutic or prophylactic dose. A broader definition of ADRs was also applied, which included the Y40–59 codes as well as diagnosis codes that have a very high or high probability of being ADR related (category A) and others with a lower probability of being ADRs (categories B–D).

Clinical events that occurred prior to hospital admission were included if the individual received treatment for the event during the hospital stay. For example, a fall resulting in a wrist fracture that occurred 3 days prior to the individual's admission would be included if they received analgesia for the fracture during their hospital stay.

2.5 | Medication use at admission and discharge

Data were recorded on medication use, including drug name, active ingredient(s), Anatomical Therapeutic Classification code, dose, frequency and duration. Information was collated from the Emergency Department assessment, progress notes, medication chart(s), Medication Management Plans and discharge summary for the relevant hospital stay. Admission medications were defined as the medications the individual was using prior to hospital admission. This information was collected from documentation of a best possible medication history and medication reconciliation on admission, when available. Discharge medications consisted of the continuing medications taken prior to admission (with/without dose modifications) and newly started medications being used at the time of hospital discharge. This information was collected from the discharge medication list in the discharge summary. Drug status was defined as the type of change made to the admission medications, for example, dose reduction or dose increase. Regular medications were defined as all active pharmaceutical ingredients excluding *as required* medications and selected complementary and alternative medications, including vitamins and mineral supplements, which were included on the Pharmaceutical Benefits Scheme (PBS) general schedule (last consulted on 27 August 2019) for any condition or population were considered a regular medication.

Three different measures of medication use were applied to active ingredients of each patient's regular medications on admission and discharge. The first was the number of active ingredients. This was considered as absolute number, polypharmacy (concurrent use of 5 or more) and hyperpolypharmacy (concurrent use of 10 or more) active ingredients as regular medications. The second was DBI, a

measure of the cumulative exposure of an individual's anticholinergic and sedative medications that estimates the functional burden of an older person's medications.[10] Where a regular medication contributed to DBI, the minimum effective daily dose (δ) currently recommended by the Australian Therapeutic Goods Administration and actual daily dose (D) were recorded to calculate each patient's DBI according to the formula $DBI = \Sigma \frac{D}{D+\delta}$.[11] If actual daily dose was missing, we imputed average DBI score for that medication, based on the study cohort scores at admission or discharge. Use of at least 1 DBI-contributing medication constituted exposure to DBI medications and was expressed as proportions. The third was Beer's Criteria 2015,[12] an explicit list of PIMs in older adults. Medications were considered independent of and in relation to drug–disease/syndrome interactions. The presence of at least 1 regular medication listed on the 2015 Beers criteria was used to capture exposure to PIMs. This was expressed as proportions. The number of regular PIMs per patient was also calculated.

2.6 | Statistical analyses

Stata IC (Stata Statistical Software: Release 16. College Station, TX, USA: StataCorp LLC. StataCorp) was used to perform all drug utilization and regression analyses. Descriptive statistics (means for continuous and integer variables; frequency and proportions for categorical variables) were reported for the cohort's sociodemographics, clinical characteristics, medication use and high-risk prescribing measures on admission and discharge (including the top 20 drug classes that contributed to high-risk prescribing). Changes in medication use for patients between admission and discharge were summarized by the mean of the within-person difference for the number of regular medications, DBI score and number of PIMs, based on pair *t*-tests; and within-person change in high-risk prescribing measures was summarized as change in proportions for polypharmacy, hyperpolypharmacy, DBI > 0, any exposure to PIMs, based on McNemar's χ^2 test.

Cross-sectional associations between medication use and the clinical outcomes were analysed using logistic regression with medication use fitted as a binary explanatory variable or as a continuous explanatory variable for integer or score medication use measures. All models for clinical outcomes used an offset for length of hospital stay to adjust for differences in duration of hospital stay between patients. The adjusted results presented for clinical outcomes also included the following explanatory variables in the model: age fitted as a continuous variable; sex coded as a binary variable; and the Charlson Comorbidity Index coded as a categorical variable with 4 groups (0, 1, 2, 3+).

2.7 | Cost of medications

Cost analyses were conducted using Stata 16 (StataCorp LLC, TX, USA). The costs of medications contributing to DBI score and PIMs were calculated per person per day at admission and discharge for the cohort in Australian dollars. Medications were included if they were listed on the PBS Schedule, 1 May 2020 (https://www.pbs.gov.au/pbs/home). The PBS Schedule lists all medications that are available to be dispensed to patients, at a price subsidized by the Australian Federal Government, and includes medications for most medical conditions. Costs were calculated on the basis of the Dispensed Price for Maximum Quantity, which is the PBS-listed price for dispensing the maximum quantity of a product and incorporates the approved ex-manufacturer price and all relevant dispensing fees and mark-ups. The costs of medications were calculated using the reported dosage and frequency of administration.

3 | RESULTS

In total, 2000 patients were included in this cohort study (Table 1). The mean age (± standard deviation) of patients was 86.0 (5.8) years, 59% were female, and 21% were admitted to hospital from a residential aged care facility. In this cohort, 31% of people spoke a language other than English at home, and 26% had a documented dementia diagnosis.

Use of multiple medications was very common. Number of medications increased overall from admission to discharge, with small reductions in both DBI score and use of PIMs according to the 2015 Beers criteria in the cohort (Table 2). On an individual patient level (Figure 1), 57% of patients had an increase in their number of regular prescribed medications (active ingredients), 53% had a decrease in DBI score, and 81% had a decrease in number of PIMs. The 20 medication classes that contributed most commonly to DBI score and PIMs on admission and discharge are shown in Table S1.

Adverse outcomes were common and variably associated with measures of medication exposure on admission (Figure 2 and Table 3). Falls were present on admission or occurred during the hospital stay in 34% of the cohort. Number of regular medications was not associated with falls; hyperpolypharmacy was associated with a lower risk of falls; and both DBI score and exposure to PIMs were associated with a higher risk of falls. Pressure areas were documented as present on admission or occurring during the hospital stay in 8% of the cohort; these were not associated with any of the medication measures. Delirium occurred in 25% of the cohort (22% prevalent on admission and an additional 3% occurring during the hospital stay). Number of medications, polypharmacy and hyperpolypharmacy were not associated with delirium; and both DBI score and PIMs exposure were associated with a greater risk of delirium. All measures of drug exposure were associated with an increased risk of ADRs, defined using the more specific Y codes only, and with the more sensitive Y + ABCD codes (prevalence during hospital stay 12 and 31%, respectively).

On admission, medications contributing to DBI cost $0.88 per day (95% confidence interval 0.84–1.08), with a mean increase of $0.08 per day (0.01–0.16) on discharge. On admission, PIMs cost $0.29 per day (0.26–0.34), with a mean change of −$0.02 per day (−0.05–0.02) on discharge (Table 4).

TABLE 1 Characteristics of the Towards Optimizing Hospitalized Older adults' MEdications (TO HOME) cohort.

Characteristics	Cohort ($n = 2000$)	
Age (years), mean (standard deviation)	86	(5.8)
Sex (female), *n* (%)	1181	(59)
Language spoken at home, *n* (%)		
English	1381	(69)
Language other than English	613	(31)
Country of birth, *n* (%)		
Australia	930	(47)
Italy	213	(11)
UK	120	(6)
Greece	103	(5)
China	96	(5)
Other	538	(27)
Marital status, *n* (%)		
Widowed	926	(46)
Married/de facto	765	(38)
Never married	155	(8)
Divorced/separated	144	(7)
Unknown	10	(1)
Covered by Veteran Affairs, *n* (%)	155	(8)
Number of comorbidities (Charlson Comorbidity Index), *n* (%)		
Score 0	925	(46)
Score = 1–2	740	(37)
Score = 3+	335	(17)
Cognition, *n* (%)		
Dementia status	517	(26)
Mild cognitive impairment[a]	197	(10)
End-of-life status, *n* (%)	98	(5)
Primary reason for admission,[b] *n* (%)		
Musculoskeletal or connective tissue system	517	(26)
Respiratory	322	(16)
Neurological and psychiatric	308	(15)
Cardiac and circulatory system	220	(11)
Genitourinary system	148	(7)
Gastrointestinal system	122	(6)
Dermatological	101	(5)
Infection	79	(4)
Haematological and neoplasms	61	(3)
Endocrine and metabolic disorders	35	(2)
Other	87	(4)
Service, *n* (%)		
Aged care	1139	(57)
General medicine	541	(27)
Rehabilitation	320	(16)
Living status prior to admission, *n* (%)		
Home	1458	(73)
Residential aged care facility	421	(21)

TABLE 1 (Continued)

Characteristics	Cohort ($n = 2000$)	
Assisted living	118	(6)
Other (including homeless)	3	(<1)
Discharge destination, *n* (%)		
Home	1050	(53)
Residential aged care facility	506	(25)
Private hospital	189	(9)
Public hospital	97	(5)
Assisted living	78	(4)
Respite	66	(3)
Transitional care unit	11	(1)
Hospice	1	(<1)
Other	2	(<1)

[a]Explicit documentation of a diagnosis of cognitive impairment without a formal diagnosis of dementia.
[b]Classification by body system using the ICD-10-AM code (diagnosis_codeP) submitted to the Admitted Patient Data Collection. See Table S2 for a thorough breakdown of the principal reason for admission.

TABLE 2 Medication use at admission to and discharge from hospital.

Summary of exposure		Admission[a]		Discharge[b]		Discharge—admission difference between means or percentages (95% CI)
Active ingredients	Mean (SD)	7.6	(4.2)	8.7	(4.2)	1.05 (0.92–1.18)
Polypharmacy[a]	*n* (%)	1543	(77)	1675	(84)	6.6 (4.8–8.4)
Hyperpolypharmacy[b]	*n* (%)	583	(29)	810	(41)	11.4 (9.3–13.4)
DBI drugs						
Any exposure	*n* (%)	1068	(53)	1104	(55)	1.8 (0.05–3.5)
Score (continuous)	Mean (SD)	0.48	(0.63)	0.46	(0.58)	−0.02 (−0.04 to −0.01)
Beers criteria drugs						
Any exposure	*n* (%)	670	(34)	595	(30)	−3.8 (−5.4 to −2.1)
Number (continuous)	Mean (SD)	0.47	(0.79)	0.40	(0.72)	−0.07 (−0.09 to −0.04)

Abbreviations: DBI, Drug Burden Index; SD, standard deviation.
[a]Polypharmacy, ≥5 regular active ingredients.
[b]Hyperpolypharmacy, ≥10 regular active ingredients (a subset of polypharmacy).

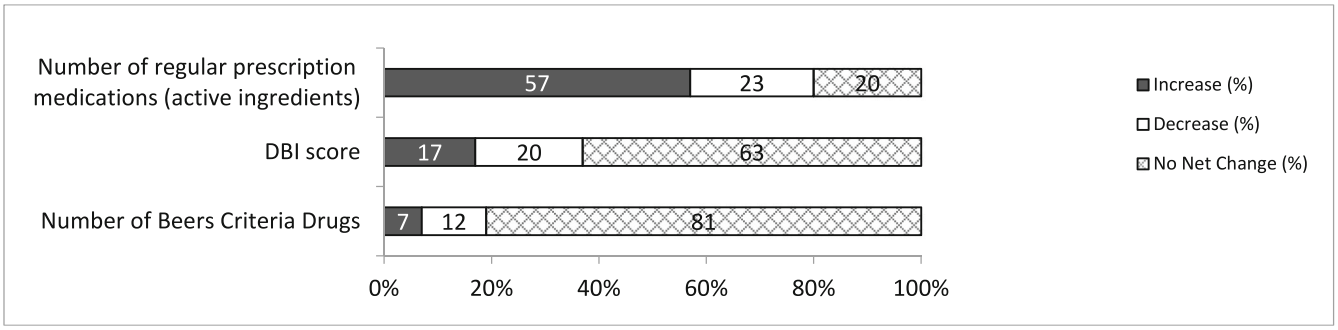

FIGURE 1 Prevalence of change in the number of medications, the Drug Burden Index (DBI) score and number of Beers criteria drugs between admission and discharge at an individual participant level ($n = 2000$).

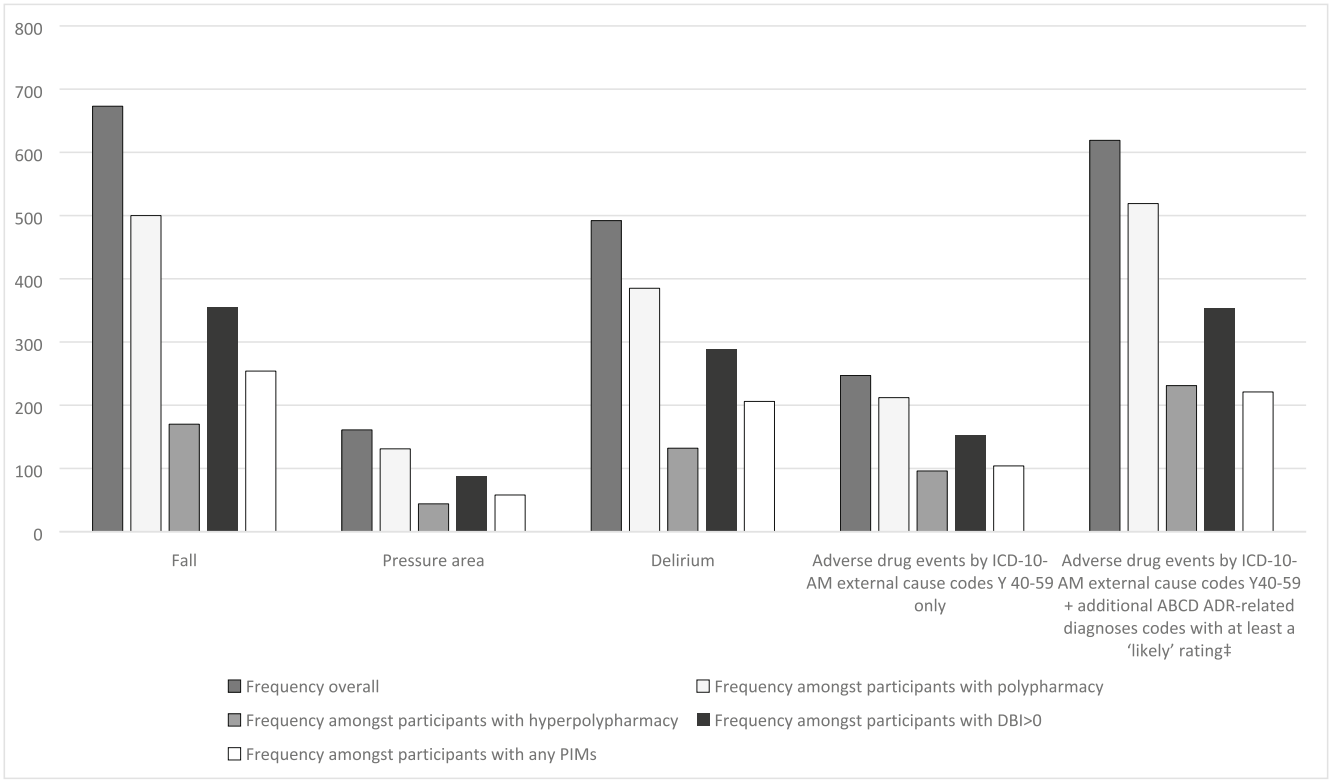

FIGURE 2 Frequency of adverse outcomes in older inpatients overall and amongst subgroups exposed to different measures of high-risk prescribing. DBI, Drug Burden Index; PIMs, potentially inappropriate medications. ‡Consists of causality ratings A1, A2, B, C and D as defined by Du et al.[9]

4 | DISCUSSION

In this unique real-world inpatient cohort of 2000 older adults consecutively admitted to 6 diverse Australian hospitals, use of multiple medications was common and increased during the hospital stay. However, the DBI score, a measure of medication risk in older adults that includes drug class and dose, and use of Beers criteria PIMs, which consider medication class with dose or indication in some circumstances, both decreased from admission to discharge. This was seen consistently in measures at a cohort level and an individual level. The DBI score and PIM exposure, but not total number of drugs used, were associated with an increased risk of falls and delirium. Number of drugs, the DBI score and PIMs were all associated with an increased risk of adverse drug events in hospital. The direct cost of medications contributing to the DBI or Beers criteria is very low.

The high exposure of this inpatient population to polypharmacy, anticholinergic and sedative drugs and PIMs and the very small changes seen during the hospital stay are comparable to findings in previous observational studies in Australia and internationally.[7,13,14] Deprescribing interventions in hospital have shown small impacts on prescribing outcomes.[15] Barriers to implementing medication review and deprescribing in hospital practice are well described,[16] with additional complexity in communication with our cohort arising from the high prevalence of people with cognitive impairment and from non-English-speaking backgrounds.

The prevalence of ADRs that caused admission or occurred during the hospital stay was 12–31%, depending on ICD-10-AM definition used. This is comparable to the estimates from systematic reviews and meta-analyses of studies of hospitalized older people, of 16% (95% confidence interval 12–22%) for in hospital ADRs[17] and 8.7% (7.6–9.8%) for hospital admissions caused by ADRs.[18] The association of polypharmacy with an increased risk of ADRs is consistent with previous reports demonstrating that number of drugs is a strong predictor of in hospital ADRs[19] and of ADRs causing hospital admissions.[18] While our study demonstrated an increased risk of ADRs with use of PIMs, only a minority of ADRs that occur in hospital[20] or cause hospital admission[21] are attributable to PIMs, and only 1 of 6 studies in a recent review found a significant relationship between PIMs and hospital admissions due to ADRs in older inpatients.[18] Our study also demonstrated an association of DBI with ADRs. To our knowledge, this explicit relationship has not been reported previously.

The lack of association of polypharmacy with falls or delirium in our inpatient cohort contrasts with much of the existing literature. Much of the data for the association of polypharmacy with falls are from community-dwelling older adults[22] or nursing homes,[23] and there are limited data specifically on polypharmacy as a risk factor for falls or delirium causing hospital admission or occurring in hospital.[24–26] The association of specific drug classes, many of which are captured by DBI and Beers criteria, with falls and delirium is better

TABLE 3 Association of high-risk medication exposures with adverse outcomes that were present on admission or developed during stay in hospital.

Adverse outcomes	Exposures (frequency, odds ratio, 95% confidence interval)							
		Number of medications			DBI-contributing drug exposure (DBI > 0)	DBI score (continuous variable	Beers drugs (PIMs) exposure	Number of Beers drugs (PIMs)
		Total number of active ingredients	Polypharmacy	Hyperpolypharmacy				
Falls	Unadjusted	0.96 (0.95,1.13)	0.73 (0.59,0.89)	0.71 (0.57, 0.89)	1.03 (0.84, 1.26)	1.06 (0.91,1.23)	1.49 (1.21, 1.83)	1.27 (1.13, 1.44)
	Adjusted	0.97 (0.94,1.00)	0.79 (0.60,1.04)	0.76 (0.60, 0.97)	1.14 (0.90,1.44)	1.21 (1.00, 1.46)	1.63 (1.28, 2.08)	1.63 (1.28, 2.08)
Pressure areas	Unadjusted	1.01 (0.97, 1.05)	1.29 (0.84, 1.97)	0.90 (0.62, 1.31)	1.16 (0.83, 1.62)	1.11 (0.85, 1.46)	1.24 (0.88, 1.76)	1.21 (0.99, 1.47)
	Adjusted	1.00 (0.97, 1.05)	1.28 (0.83, 1.97)	0.93 (0.64, 1.36)	1.14 (0.81, 1.62)	1.12 (0.85, 1.49)	1.23 (0.87, 1.78)	1.19 (0.97, 1.45)
Delirium	Unadjusted	1.00 (0.97, 1.02)	1.08 (1.03, 1.40)	0.92 (0.72, 1.16)	1.48 (1.19, 1.83)	1.45 (1.23, 1.71)	1.89 (1.52, 2.36)	1.48 (1.30, 1.68)
	Adjusted	1.01 (0.96, 1.04)	1.22 (0.92, 1.62)	1.07 (0.82, 1.38)	1.25 (0.96, 1.57)	1.42 (1.19, 1.71)	1.76 (1.38, 1.46)	1.42 (1.23, 1.63)
Adverse drug events by ICD-10-AM external cause codes Y 40–59 only	Unadjusted	1.08 (1.05, 1.12)	1.94 (1.32, 2.86)	1.74 (1.30, 2.32)	1.69 (1.27, 2.25)	1.79 (1.47, 2.18)	1.73 (1.30, 2.30)	1.34 (1.14, 1.58)
	Adjusted	1.08 (1.05, 1.12)	1.98 (1.33, 2.93)	1.76 (1.31, 2.36)	1.83 (1.36, 2.44)	1.90 (1.55, 2.15)	1.87 (1.40, 2.49)	1.41 (1.19, 1.66)
Adverse drug events by ICD-10-AM external cause codes Y40–59 + additional ABCD ADR-related diagnoses codes with at least a *likely* rating[a]	Unadjusted	1.10 (1.07, 1.12)	1.89 (1.46, 2.46)	1.88 (1.51, 2.33)	1.38 (1.13, 1.70)	1.43 (1.22, 1.67)	1.27 (1.02, 1.57)	1.14 (1.00, 1.30)
	Adjusted	1.07 (1.04, 1.11)	1.88 (1.30, 2.72)	1.63 (1.22, 2.17)	1.78 (1.34, 2.35)	1.78 (1.46, 2.17)	1.92 (1.46, 2.54)	1.40 (1.19, 1.63)

Note: Adjusted models are adjusted for age, sex and Charlson Comorbidity Index.

Abbreviations: DBI, Drug Burden Index; ICD-10-AM, International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification; PIMs, potentially inappropriate medications.

[a]Consists of causality ratings A1, A2, B, C and D as defined by Du et al.[9]

TABLE 4 Daily cost of medications (per person) contributing to Beer's criteria potentially inappropriate medications (PIMs) or Drug Burden Index (DBI) on admission to and discharge from hospital.

Total daily medication cost (per person) ($)		Admission (95% CI)	Discharge (95% CI)	Change between admission and discharge	*P* value
	DBI	0.88 (0.77–0.99)	0.96 (0.84–1.08)	0.08 (0.01–0.16)	.03
	Beers criteria PIMs	0.29 (0.26–0.34)	0.28 (0.25–0.31)	−0.02 (−0.05–0.02)	.32

Note: Medication cost is provided in Australian dollars per person per day.
Abbreviations: CI, confidence interval; DBI, Drug Burden Index; PIMs, potentially inappropriate medications.

understood.[27,28] DBI has previously been associated with falls[29,30] and fractures[31] in population based studies and with delirium in a small cohort of older inpatients.[7] Beers criteria include specific lists of drugs to avoid in people with delirium or falls,[12] which probably contributed to the observed association of Beers criteria with delirium and falls in this study.

The strengths of this study are the population size and its representativeness of older patients in metropolitan Australian hospitals. It is not representative of those who die during their hospital stay. Exclusion of patients who died in hospital is a potential source of selection bias in analysis of the association between medication use and adverse outcomes. Furthermore, the data for medication exposure and clinical characteristics were derived from detailed chart review by clinician researchers and had good inter-rater reliability. The ADR outcome is limited to a previously validated method using ICD-based criteria for ADR-related hospitalizations.[9] This is not the gold standard for collecting data on ADRs, but was selected for feasibility in this large data set. This may result in under-estimation of ADRs, particularly in older people where ADRs may present non-specifically as falls or confusion, and a bias towards ADRs that can be detected by these criteria. Future studies will investigate the sensitivity and specificity of this method for ADR detection against the gold standard of independent medical record review. While the medication history on admission captured medications taken prior to admission, and the outcomes were those present on admission and occurring during admission, some outcomes measured may have been sub-acute or chronic, preceding medication changes made prior to admission. The associations between drug use and outcomes are likely to be limited by residual confounding. The data quality was not considered strong enough for all elements in the causative pathways to obtain estimates of attributable risk for costing of health outcomes with medication use. Future studies will link this inpatient cohort with detailed clinical and prescribing data to longitudinal administrative data on readmission, mortality and medication use.

5 | CONCLUSIONS

Multiple medication use is very common in older inpatients, with some reduction of high-risk medication exposures during usual care. While optimal medication regimens for older individuals may include some use of anticholinergic and sedative medications (DBI > 0) and occasional use of PIMs, the substantial exposure to these medications on discharge suggests that there is scope to improve medication review during a hospital stay. While the costs of the drugs contributing to DBI and Beers criteria are low, the costs of the associated falls, delirium and ADRs also need to be considered.

AUTHOR CONTRIBUTIONS

Sarah Hilmer conceptualized the study, supervised design, acquisition of data, analysis and interpretation of data, drafted the manuscript and revised after consideration of input from coauthors, gave final approval of the version to be published, and is accountable for all aspects of the work. Sarita Lo contributed to the design of the study, led acquisition of data, assisted with analysis, revised manuscript and approved the final version. Patrick Kelly contributed to design of the study, led analysis, revised the manuscript and approved the final version. Rosalie Viney contributed to the conceptualization and design of the study, supervised the economic analysis, revised the manuscript, and approved the final version. Fiona Blyth, David Le Couteur and Andrew McLachlan contributed to the conceptualization and design of the study, contributed to the interpretation of data, revised the manuscript, and approved the final version. Sheena Arora and Lutfun Hossain contributed to the design of the economic analysis, conducted the economic analysis, contributed to the interpretation of data, revised the manuscript and approved the final version. Danijela Gnjidic contributed to the conceptualization and design of the study, contributed to the acquisition, analysis and interpretation of data, revised the manuscript, and approved the final version.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge assistance with data collection from Sharon Chen, Linda Koria, Bonnie Liu, Mitchell Redston and Marissa Sakiris. We acknowledge assistance with the Sydney Local Health District Electronic Medical Record from Rosemary Bourke and with data management from Terry Jin, Jessica Nguyen and Meggie Zhang. We acknowledge assistance with data analysis provided Juliet Byrnes, Sydney School of Public Health, Faculty of Medicine and Health, The University of Sydney. Open access publishing facilitated by The University of Sydney, as part of the Wiley - The University of Sydney agreement via the Council of Australian University Librarians.

CONFLICT OF INTEREST STATEMENT

None of the authors declare any conflicts of interest relevant to this paper.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request, within privacy/ethical restrictions.

ORCID

Sarah N. Hilmer https://orcid.org/0000-0002-5970-1501

Danijela Gnjidic https://orcid.org/0000-0002-9404-3401

REFERENCES

1. Institute for Healthcare Improvement. Age-friendly health systems: guide to using the 4Ms in the care of older adults. 2020. https://www.ihi.org/Engage/Initiatives/Age-Friendly-Health-Systems/Documents/IHIAgeFriendlyHealthSystems_GuidetoUsing4MsCare.pdf. Accessed 20/12/2022.
2. Hubbard RE, Peel NM, Scott IA, et al. Polypharmacy among inpatients aged 70 years or older in Australia. *Med J Aust*. 2015;202(7):373-377. doi:10.5694/mja13.00172
3. Alhawassi TM, Krass I, Bajorek BV, Pont LG. A systematic review of the prevalence and risk factors for adverse drug reactions in the elderly in the acute care setting. *Clin Interv Aging*. 2014;9:2079-2086. doi:10.2147/CIA.S71178
4. Long SJ, Brown KF, Ames D, Vincent C. What is known about adverse events in older medical hospital inpatients? A systematic review of the literature. *International J Qual Health Care*. 2013;25(5):542-554. doi:10.1093/intqhc/mzt056
5. Hilmer SN, McLachlan AJ, Le Couteur DG. Clinical pharmacology in the geriatric patient. *Fundam Clin Pharmacol*. 2007;21(3):217-230. doi:10.1111/j.1472-8206.2007.00473.x
6. 45 and Up Study Collaborators, Banks E, Redman S, et al. Cohort profile: the 45 and up study. *Int J Epidemiol*. 2008;37(5):941-947. doi:10.1093/ije/dym184
7. Best O, Gnjidic D, Hilmer SN, Naganathan V, McLachlan AJ. Investigating polypharmacy and drug burden index in hospitalised older people. *Intern Med J*. 2013;43(8):912-918. doi:10.1111/imj.12203
8. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghali WA. New ICD-10 version of the Charlson comorbidity index predicted in-hospital mortality. *J Clin Epidemiol*. 2004;57(12):1288-1294. doi:10.1016/j.jclinepi.2004.03.012
9. Du W, Pearson SA, Buckley NA, Day C, Banks E. Diagnosis-based and external cause-based criteria to identify adverse drug reactions in hospital ICD-coded data: application to an Australia population-based study. *Public Health Res Pract*. 2017;27(2):e2721716. doi:10.17061/phrp2721716
10. Hilmer SN, Mager DE, Simonsick EM, et al. A drug burden index to define the functional burden of medications in older people. *Arch Intern Med*. 2007;167(8):781-787. doi:10.1001/archinte.167.8.781
11. Hilmer SN, Gnjidic D, Abernethy DR. Drug burden index for international assessment of the functional burden of medications in older people. *J Am Geriatr Soc*. 2014;62(4):791-792. doi:10.1111/jgs.12707
12. By the American Geriatrics Society Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated beers criteria for potentially inappropriate medication use in older adults. *J am Geriatr Soc*. 2015;63(11):2227-2246. doi:10.1111/jgs.13702
13. Chan B, Reeve E, Matthews S, et al. Medicine information exchange networks among healthcare professionals and prescribing in geriatric medicine wards. *Br J Clin Pharmacol*. 2017;83(6):1185-1196. doi:10.1111/bcp.13222
14. Gallagher P, Lang PO, Cherubini A, et al. Prevalence of potentially inappropriate prescribing in an acutely ill population of older patients admitted to six European hospitals. *Eur J Clin Pharmacol*. 2011;67(11):1175-1188. doi:10.1007/s00228-011-1061-0
15. Thillainadesan J, Gnjidic D, Green S, Hilmer SN. Impact of deprescribing interventions in older hospitalised patients on prescribing and clinical outcomes: a systematic review of randomised trials. *Drugs Aging*. 2018;35(4):303-319. doi:10.1007/s40266-018-0536-4
16. Dalton K, O'Mahony D, Cullinan S, Byrne S. Factors affecting prescriber implementation of computer-generated medication recommendations in the SENATOR trial: a qualitative study. *Drugs Aging*. 2020;37(9):703-713. doi:10.1007/s40266-020-00787-6
17. Jennings ELM, Murphy KD, Gallagher P, O'Mahony D. In-hospital adverse drug reactions in older adults; prevalence, presentation and associated drugs-a systematic review and meta-analysis. *Age Ageing*. 2020;49(6):948-958. doi:10.1093/ageing/afaa188
18. Oscanoa TJ, Lizaraso F, Carvajal A. Hospital admissions due to adverse drug reactions in the elderly. A meta-analysis. *Eur J Clin Pharmacol*. 2017;73(6):759-770. doi:10.1007/s00228-017-2225-3
19. Onder G, Petrovic M, Tangiisuran B, et al. Development and validation of a score to assess risk of adverse drug reactions among in-hospital patients 65 years or older: the GerontoNet ADR risk score. *Arch Intern Med*. 2010;170(13):1142-1148. doi:10.1001/archinternmed.2010.153
20. Corsonello A, Pedone C, Lattanzio F, et al. Potentially inappropriate medications and functional decline in elderly hospitalized patients. *J am Geriatr Soc*. 2009;57(6):1007-1014. doi:10.1111/j.1532-5415.2009.02266.x
21. Budnitz DS, Lovegrove MC, Shehab N, Richards CL. Emergency hospitalizations for adverse drug events in older Americans. *N Engl J Med*. 2011;365(21):2002-2012. doi:10.1056/NEJMsa1103053
22. Tromp AM, Pluijm SM, Smit JH, Deeg DJ, Bouter LM, Lips P. Fall-risk screening test: a prospective study on predictors for falls in community-dwelling elderly. *J Clin Epidemiol*. 2001;54(8):837-844. doi:10.1016/S0895-4356(01)00349-3
23. Neutel CI, Perry S, Maxwell C. Medication use and risk of falls. *Pharmacoepidemiol Drug Saf*. 2002;11(2):97-104. doi:10.1002/pds.686
24. Oliver D, Daly F, Martin FC, McMurdo ME. Risk factors and risk assessment tools for falls in hospital in-patients: a systematic review. *Age Ageing*. 2004;33(2):122-130. doi:10.1093/ageing/afh017
25. Oliveira JESL, Berning MJ, Stanich JA, et al. Risk factors for delirium in older adults in the emergency department: a systematic review and meta-analysis. *Ann Emerg Med*. 2021;78(4):549-565. doi:10.1016/j.annemergmed.2021.03.005
26. Heinrich M, Nottbrock A, Borchers F, et al. Preoperative medication use and development of postoperative delirium and cognitive dysfunction. *Clin Transl Sci*. 2021;14(5):1830-1840. doi:10.1111/cts.13031
27. Hartikainen S, Lonnroos E, Louhivuori K. Medication as a risk factor for falls: critical systematic review. *J Gerontol A Biol Sci Med Sci*. 2007;62(10):1172-1181. doi:10.1093/gerona/62.10.1172
28. Han QYC, Rodrigues NG, Klainin-Yobas P, Haugan G, Wu XV. Prevalence, risk factors, and impact of delirium on hospitalized older adults with dementia: a systematic review and meta-analysis. *J Am Med Dir Assoc*. 2022;23(1):23-32 e27. doi:10.1016/j.jamda.2021.09.008
29. Jamieson HA, Nishtala PS, Scrase R, et al. Drug burden and its association with falls among older adults in New Zealand: a national population cross-sectional study. *Drugs Aging*. 2018;35(1):73-81. doi:10.1007/s40266-017-0511-5
30. Nishtala PS, Narayan SW, Wang T, Hilmer SN. Associations of drug burden index with falls, general practitioner visits, and mortality in older people. *Pharmacoepidemiol Drug Saf*. 2014;23(7):753-758. doi:10.1002/pds.3624

31. Jamieson HA, Nishtala PS, Scrase R, et al. Drug burden index and its association with hip fracture among older adults: a National Population-Based Study. *J Gerontol A Biol Sci Med Sci*. 2019;74(7):1127-1133. doi:10.1093/gerona/gly176

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Hilmer SN, Lo S, Kelly PJ, et al. Towards Optimizing Hospitalized Older adults' MEdications (TO HOME): Multi-centre study of medication use and outcomes in routine care. *Br J Clin Pharmacol*. 2023;89(8):2508-2518. doi:10.1111/bcp.15727