

# Associations between potentially inappropriate prescribing and increased number of medications with post-discharge health outcomes among geriatric rehabilitation inpatients: RESORT study

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## Abstract

**Aims:** Older adults are vulnerable to medication-related harm mainly due to high use of medications and inappropriate prescribing. This study aimed to investigate the associations between inappropriate prescribing and number of medications identified at discharge from geriatric rehabilitation with subsequent post-discharge health outcomes. **Method:** REStORing health of acutely unwell adults (RESORT) is an observational, longitudinal cohort study of geriatric rehabilitation inpatients. Potentially inappropriate medications (PIMs) and potential prescribing omissions (PPOs) were measured at acute admission, and at admission and discharge from geriatric rehabilitation, using version 2 of the STOPP/START criteria. **Results:** 1890 patients (mean age  $82.6 \pm 8.1$  years, 56.3 % females) were included. The use of at least 1 PIMs, or PPOs at geriatric rehabilitation discharge were not associated with 30-day and 90-day readmission and 3-month and 12-month mortality. Central nervous system (CNS)/psychotropics and fall risk PIMs were significantly associated with 30-day hospital readmission (adjusted odds ratio (AOR) 1.53; 95%CI 1.09-2.15), and cardiovascular PPOs with 12-month mortality (AOR 1.34; 95%CI 1.00-1.78). Increased number of discharge medications was significantly associated with 30-day (AOR 1.03; 95%CI 1.00-1.07) and 90-day (AOR 1.06; 95%CI 1.03-1.09) hospital readmissions. The use and number of PPOs (including vaccine omissions) were associated with reduced independence in instrumental activities of daily living scores at 90-days post geriatric rehabilitation discharge. **Conclusion:** The number of discharge medications, CNS/psychotropics and fall risk PIMs were significantly associated with readmission, and cardiovascular PPOs with mortality. Interventions are needed to improve appropriate prescribing in geriatric rehabilitation patients to prevent hospital readmission and mortality.

## Introduction

Medication-related harm is an underdiagnosed problem in Australia,<sup>1</sup> costing the Australian healthcare system about A\$1.4 billion per annum.<sup>2</sup> The older population (aged [?]65 years) is particularly vulnerable to medication-related harm due to their advanced age, multimorbidity and increased use of medications (polypharmacy).<sup>3</sup> Increased medication use is, in turn, linked to potentially inappropriate prescribing (PIP).<sup>4,5</sup> Potentially inappropriate prescribing comprises the use of potentially inappropriate medications (PIMs) where the risks outweigh clinical benefits and potential prescribing omissions (PPOs), which is the failure to prescribe medications that provide benefits.<sup>6</sup> Recent reviews have shown that PIPs are common among older adults in diverse healthcare settings, and are associated with medication-related hospitalisation, adverse drug reactions, adverse drug events, and functional decline.<sup>7,8</sup> A systematic review and meta-analysis of 63 included studies has shown that patients using at least 1 PIM in the inpatient setting (compared with

non-users) were associated with a 91% increased odds of medication-related hospital admission, and 60% increased odds of dependency in at least 1 activity of daily living.<sup>7</sup>

Multiple screening tools are available to detect and reduce PIPs among older adults, such as the Screening Tool of Older Person's Prescriptions and the Screening Tool to Alert doctors to Right Treatment (STOPP/START) criteria, and the Beers criteria.<sup>9</sup> These are also the tools commonly used in research in Australian healthcare setting.<sup>10-14</sup> PIP, according to STOPP/START criteria, have been investigated mainly through retrospective analysis in acute care settings,<sup>11-13</sup> with high variability in prevalence estimates between care transition points. A clinical audit of electronic medical records of 249 older people from an Australian teaching hospital found 51% were exposed to at least 1 PIM at hospital admission and, this prevalence was reduced to 37% at discharge.<sup>12</sup> In contrast, another Australian study found an increase in the prevalence of PIM use from hospital admission to discharge (54.8% vs 60.8%).<sup>13</sup> In addition, results from previous international studies on the influence of inappropriate prescribing on post-discharge health outcomes are mixed. While some studies highlighted the presence of PIMs/PPOs was significantly associated with potentially preventable medication-related hospital admissions,<sup>15</sup> repeated hospital admissions and mortality,<sup>16</sup> other investigations did not confirm these findings with respect to post-discharge health outcomes, including rehospitalization and mortality either in acute care<sup>17-19</sup> or geriatric rehabilitation settings.<sup>20</sup> Moreover, evidence is limited on PIM/PPO prevalence as well as their associations with post-discharge health outcomes in patients admitted to and discharged from geriatric rehabilitation settings.

The purpose of this study was to assess the prevalence of PIM and PPO use at transitions of geriatric rehabilitation care (acute admission, admission to and discharge from geriatric rehabilitation) and to investigate the associations between PIMs, PPOs, and number of medications identified at discharge from geriatric rehabilitation with subsequent post-discharge health outcomes, including hospital readmissions and mortality.

## Methods

**Study design and setting:** RESORT (REStOring health of acutely unwell adultTs) is an observational longitudinal study cohort of patients admitted to the Royal Melbourne Hospital (Victoria, Australia) for geriatric rehabilitation (recruitment commenced October 16, 2017, and ended March 18, 2020), comprising a total of 1890 older adults. A description of the cohort, methods, and design in the RESORT study is available elsewhere.<sup>21,22</sup> Briefly, patients on the geriatric rehabilitation wards of the Royal Melbourne Hospital, Melbourne, Australia, completed a standardized comprehensive geriatric assessment at both admission and discharge by a multidisciplinary team inclusive of physicians, nurses, physiotherapists, and occupational therapists, and followed up at 3 months post-discharge via phone interviews. Written informed consent was obtained by all patients or a nominated proxy. Patients were excluded if they were receiving palliative care at admission, were transferred to acute care prior to consenting to the study or lacked both the capacity to provide informed consent and a nominated proxy. The study was approved by the Melbourne Health Human Research Ethics Committee (HREC/17/MH/103).

**Data sources and collection:** Age, sex, and length of stay were obtained from medical records. Other demographic characteristics (e.g., current living situation, living status, primary language, walking ability) were obtained from a survey completed by the patient and/or carer. The primary reason for hospital admission was extracted from medical records and grouped into musculoskeletal, neurological, cardiorespiratory, infection and other (including gastrological, urology, hematology, ophthalmology, vascular, psychiatry related conditions, cancer, and metabolic disorders) by trained researchers. Physicians assessed morbidity using the Charlson Comorbidity Index (CCI)<sup>23</sup> and the Cumulative Illness Rating Scale (CIRS).<sup>24</sup> CCI and CIRS scores ranged from 0-37 and 0-56, respectively. Frailty was assessed by physicians using the Clinical Frailty Scale (CFS),<sup>25</sup> ranging from 1-9, with greater scores indicating a higher level of frailty. Cognitive impairment assessment was completed by physicians and was defined as a dementia diagnosis captured by the CCI, CIRS, or medical records, or a score on the Standardized Mini-Mental State Examination of < 24 points,<sup>26</sup> Montreal Cognitive Assessment score < 26 points,<sup>27</sup> or the Rowland Universal Dementia Scale < 23 points.<sup>28</sup> Functional independence status was examined by occupational therapists using the Katz Acti-

vities of Daily Living (ADL) <sup>29</sup> and Lawton and Brody Instrumental Activities of Daily Living (IADL)<sup>30</sup> on admission and at discharge from geriatric rehabilitation. Scores of ADLs and IADL ranged between 0–6 and 0–8 points, respectively, with higher scores indicating higher level of independence. ADL and IADL scores at three months post-discharge were assessed by trained researchers via telephone interview with the patient and/or carer. All types of medications (chronic, acute, over the counter) that patients were taking across the care transitions (acute admission, admission to and discharge from geriatric rehabilitation wards) were extracted from medical records.

*Potentially inappropriate medications:* PIMs and PPOs were quantified according to version 2 of the Screening Tool of Older People’s Prescription (STOPP) and the Screening Tool to Alert Doctors to the Right Treatment (START) criteria, respectively.<sup>6</sup> These explicit screening tools, developed using expert opinion using available evidence from literature and clinical guidelines, consisted of 80 STOPP and 34 START items to identify unnecessary medications and omitted medications, respectively. PIMs/PPOs were identified across the three care transitions (acute admission, on admission to and at discharge from geriatric rehabilitation ward) during geriatric rehabilitation care. The data were extracted by a qualified pharmacist, with regular independent checks by another qualified pharmacist.

*Outcome variables:* The primary outcomes of interest were hospital readmissions, and mortality after hospital discharge. Readmission was defined as an unplanned acute readmission after discharge and was obtained from medical records and at 3-month phone interviews. Mortality was defined as death of patient at 3- or 12-months post-discharge and was obtained from the Registry of Births, Deaths and Marriages Victoria and medical records. The secondary outcome was functional status at 3-months post discharge from geriatric rehabilitation.

*Data analysis:* Descriptive statistics was undertaken to summarize the main characteristics of older patients. Continuous variables were reported as mean with corresponding standard deviation, or median with interquartile ranges if not normally distributed. Categorical variables were reported as absolute frequencies and percentages. The prevalence of PIPs (PIM/PPO) was calculated as a ratio between the number of patients exposed to at least 1 PIP (PIM/PPO) and the total number of patients included. To investigate the associations between PIPs identified at discharge and subsequent outcomes (e.g., hospital readmission, mortality, functional outcomes), PIPs were measured as a dichotomous variable (yes/no), as well as a continuous variable (number of PIPs). Only patients discharged alive were considered in the estimations related to analyses involving associations between PIPs and post-discharge health outcomes. For comparison between PIP and outcome variables, Chi-square test were employed for categorical/dichotomous variables, and the independent t-test was used for continuous variables. The McNemar and Cochran’s Q tests were used to compare the prevalence of PIM/PPO between two and three care transitions, respectively. Multivariate logistic regression analyses were employed to identify the independent associations between discharge PIMs/PPOs, and number of discharge medications with primary health outcomes. Multivariate regression analyses were further applied on PIM categories, and it was undertaken by merging similar PIMs together (e.g., Groups B and C, Groups D and K), Group A (indication) and fewer PIMs (E-J, L, M). Similarly, PPOs were categorised as Group A (cardiovascular medications), Group I (Vaccines) and other groups (B-D, F-H) and their associations were assessed against the primary outcomes. Linear regression analyses were used to determine the associations between discharge PIMs/PPOs and secondary outcomes (i.e., ADL and IADL). All multivariate analyses were adjusted for age, Charlson comorbidity index (CCI), cognitive impairment, length of stay during geriatric rehabilitation and number of discharge medications.

## Results

### Patient characteristics

Table 1 shows the patients’ characteristics on admission to geriatric rehabilitation and outcomes during hospital stay and following discharge from geriatric rehabilitation. The mean age was 82.6 years and 56.3% were female. Approximately, 72% of patients used a walking aid and the median frailty and Charlson comorbidity scores were 6 [5 – 7] and 2 [1 – 4], respectively. The primary reasons for hospital admissions were musculoske-

letal disorders (47%), followed by neurological disorders (15%). More than 60% of the patients had cognitive impairment and the median CIRS score was 12 [9 – 16]. Mortality rate at 3 months was 7.1% and 19.4% died at 12 months. The 30- and 90-day all-cause readmissions rates were 14.8% and 23.7%, respectively.

### PIMs and PPO prevalence

At discharge from a geriatric rehabilitation ward, a total of 18,704 medications were prescribed. The most frequently prescribed medications were analgesics (80.9%), cardiovascular medications (72.2%), vitamin D (61.1%) and psychotropics (50.8%) (*Appendix I*).

A total of 1856 PIMs and 1368 PPOs (4482 PPOs including vaccines) were identified (*Appendix II*). The percentage of patients with at least one PIM was 61.6% on acute admission, 58.8% on admission to geriatric rehabilitation and 54.8% at discharge from geriatric rehabilitation. The percentage of patients with at least one PPO was 91.8% on acute admission, 91.6% on admission to geriatric rehabilitation and 90.8% at discharge from geriatric rehabilitation. However, on excluding vaccine data, patients with at least 1 PPO reduced to 51.9%, 51.4% and 46.3%, respectively. There was a significant change in the prevalence of any PIM use across the care transitions (acute admission, admission to and discharge from geriatric rehabilitation), as was with the use of PPOs but without vaccine data. However, the reduction rate was consistent when the use of any PIMs or PPOs were compared between acute admission and geriatric rehabilitation discharge (*Appendix III*).

### Association of inappropriate prescribing with outcome variables

Table 2 reports the associations between the occurrence of at least one PIM or PPO or PIP identified at geriatric rehabilitation discharge with patient and disease characteristics, and outcomes. Patients with at least one PIM or PIP were significantly more likely to be discharged on higher number of medications, or to have greater than 10 discharge medications (hyper polypharmacy) and were mainly admitted due to cardiovascular diseases. Patients with at least 1 PIM, PPO or PIP were more common in patients with opioid, anti-inflammatory, Immunomodulatory and analgesic prescriptions, and with a greater burden of co-morbidities. Patients with at least 1 PPO were most likely admitted due to musculoskeletal disorders and were using walking aids. PIMs were less prevalent in older age, in patients with cognitive impairment and with longer hospitalisation.

Table 3 provides adjusted and crude ORs of the associations between inappropriate prescribing identified at geriatric rehabilitation discharge and outcome variables. On a univariate analysis, patients with at least 1 PIM and PIP were associated with an increased odds of hospital readmissions at longer follow up (i.e., 3 month), but not at 30 days of follow-up. A similar association was also evident for these outcomes when considering the numbers of PIMs and PIPs as a continuous variable. In addition, PIPs and PPOs as continuous variables also demonstrated a significant association with mortality data collected at 3 month and 12 months of follow-up.

After adjustment for confounding variables, exposure to at least 1 PIM, PPO and PIP did not show a significant association with post-discharge health outcomes. However, the number of discharge medications were significantly associated with hospital readmission at 30-days and 90-days follow-up. The prescription of each additional medication at discharge from geriatric rehabilitation increased the odds of hospital readmission by 1.04 (AOR 1.04; 95% CI 1.01-1.07) and 1.06 (AOR 1.06; 95% CI 1.03 -1.09) at 30-days and 90-days post-discharge, respectively. Specifically, patients discharged with at least 1 cardiovascular medication showed a significant increased odds of hospital readmissions at 30-days (AOR 1.43; 95% CI 1.03-1.98) and 90-days of follow-up (AOR 1.45; 95% CI 1.10-1.89). Conversely, patients whose cardiovascular PPOs were omitted at discharge from geriatric rehabilitation were associated with 12-month mortality (AOR 1.34; 95% CI 1.00-1.78) although this was not evident for mortality and other outcomes collected at shorter follow-up (Table 4). PPOs related to CVD medications were mainly due to failure to prescribe or continue use of beta-blockers in patients with ischaemic heart disease, angiotensin converting enzyme inhibitors (ACEIs) in patients with systolic heart failure and/or documented coronary artery disease and statin therapy in patients with a documented history of coronary, cerebral or peripheral vascular disease with substantial life expectancy. On

the other hand, PIMs related to CNS/psychotropics and fall risk increasing medications were significantly associated with the 30-day hospital readmission (AOR 1.53; 95% CI 1.09 - 2.15).

Linear regression analyses of the association between discharge PIMs or PPOs and the longitudinal changes of ADLs/IADLs from geriatric rehabilitation discharge to 90-days post-discharge are shown in Table 5. There was no significant association between PIMs and gains in ADLs/IADLs scores but PPO use, and specifically PPOs inclusive of vaccines negatively affected ADL/IADL gains (PPO [?] 1:  $\beta = -0.232$ , 95% -0.445 to -0.019; Number of PIPs (including vaccines):  $\beta = -0.107$ , 95% CI -0.194 to -0.021).

## Discussion

This is the first study to investigate the impact of PIMs and PPOs at discharge from geriatric rehabilitation on unplanned readmissions and mortality among geriatric rehabilitation inpatients in Australia. While the prevalence of PIM and PPO use at different time points during the transition into geriatric rehabilitation care was high, the proportion of patients taking any PIMs/PPOs significantly reduced from acute admission to geriatric rehabilitation discharge. The use of at least 1 PIMs, PPOs or PIPs at geriatric rehabilitation discharge were not associated with an increased risk of unplanned readmission and mortality, be it in the short or long-term. Specific groups of PIMs (CNS/psychotropics and fall risk increasing medications) were significantly associated with the 30-day hospital readmission and cardiovascular PPOs with the 12-month mortality. Furthermore, an increased number of discharge medications was significantly associated with 30-day and 90-day hospital readmissions. The use and number of PPOs that also included vaccine omissions were negatively associated with gains in IADL scores at 90-days following discharge from geriatric rehabilitation.

Temporal changes in the prevalence of PIMs and PPOs from acute admission to geriatric rehabilitation discharge were investigated in this study. It showed a significant reduction in PIMs and PPOs as patients moved from acute admission to discharge. While these findings were consistent with other studies,<sup>31,32</sup> there were also studies that did not show a significant difference<sup>10,33</sup> or have shown a rather increased PIM prevalence during the transition from admission to discharge.<sup>13</sup> The current study has shown that the longer that patients stayed in geriatric rehabilitation ward, the fewer patients were likely to be exposed to PIMs. Therefore, it was not surprising to see a decline in the prevalence of PIM use from acute admission to discharge in this study.

In the present study, neither PIMs, PPOs nor PIPs were shown to have an association with readmission and mortality, but a higher number of discharge medications was a major predictor for unplanned hospital readmission at 30-days following discharge from geriatric rehabilitation. This finding is not consistent with previous reports conducted in acute care,<sup>7,34</sup> in relation to hospital readmission and mortality. A recent meta-analysis highlighted the burden of medication-related harm due to potentially inappropriate prescribing.<sup>7</sup> For example, patients using at least 1 PIM use in the inpatient setting (compared with non-users) were associated with a 91% increased odds of medication-related hospital admission (AOR 1.91, 95% CI 1.21-3.01), and 60% increased odds of dependency in at least 1 ADL (AOR 1.60; 95% CI 1.28–2.01). Informed by this review, a prospective telephone follow-up study with clinical audit of electronic medical record in general medical wards was also subsequently conducted to assess the links between inappropriate medication and clinical and functional outcomes (e.g., unplanned hospital readmission, dependency in activities of daily living).<sup>34</sup> It was found that exposure to at least 1 PIM use was associated with an increased occurrence of unplanned hospital readmission (AOR 5.09; 95% CI 2.38-10.85), and there was also an increased in the likelihood of patients experiencing dependency in at least 1 ADL after hospital discharge (AOR 2.31; 95% CI 1.08-4.20).<sup>34</sup> The reason for this difference may be that related to the healthcare setting itself, in that patients admitted to geriatric rehabilitation wards stayed longer (median 19.8 days vs 5 days)<sup>34</sup> and were likely exposed to fewer PIMs than patients discharged from general medical wards. In addition, the previous study<sup>34</sup> was conducted during the intense lock down due to COVID-19 and this may have impacted healthcare provision because of understaffing. The morbidity and mortality pattern were also different – for example, 90-days readmission was 36% in a previous study<sup>34</sup> but 21.7% in the current study, it may be due to COVID-related restrictions with limited eligibility for hospital care. The lack of association between hyper polypharmacy (defined as prescription of 10 or more medications) and clinical outcomes in a previous study<sup>34</sup> may be because only

regular medications were counted unlike the current study. Medications prescribed *pro re nata*, including benzodiazepines for sleep aid may have been missed in the calculation, which was the main limitation for the previous study.<sup>34</sup> It should be noted that the prescription of psychotropic and fall risk increasing PIMs were associated with 30-day readmission in the present study.

The present results are consistent with previous studies,<sup>35,36</sup> showing that as the number of medications increase, so does the prevalence of 30-day and 90-day hospital readmissions. Basnet et al.<sup>35</sup> found that the number of discharge medications was significantly associated with increased hospital readmission within 30-days, with the risk of rehospitalization increasing by 4% for every added medication (OR 1.04; 95% CI 1.03-1.05). Another study<sup>36</sup> of 647 patients discharged from geriatric medicine acute care wards showed that taking eight or more medications was significantly associated with 90-day hospital readmission.

### Implications for practice and future research

It was encouraging to see a reduction in the prevalence of PIMs and PPOs while geriatric rehabilitation inpatients moved from acute admission to discharge but still a large proportion of patients received PIMs and PPOs at discharge from a geriatric rehabilitation. At discharge, patients may not only continue to use PIMs/PPOs from acute admission, but it may also be a site where new inappropriate medications may be introduced.<sup>37</sup> These newly added inappropriate medications conferred a higher risk of adverse events compared to chronic inappropriate medications.<sup>37</sup> Therefore, designing strategies to reduce the prescription of medications with high risk profile and tailoring deprescription practice would be an important intervention worth considering. The group of PIM medications that may be benefited from the deprescription intervention included psychotropics, fall-risk increasing drugs and other CNS acting agents. Equally important, medications that are beneficial for older people needs to be started or let them to continue at discharge and beyond. However, there should be a balance which medications to prescribe or to deprescribe – for example, in the current study, prescriptions related to CVD medications overall were associated with short-term hospital readmissions, similarly their omission has significantly increased mortality in the long-term. The better approach to optimise CVD medication use in geriatric rehabilitation inpatients is to reduce CVD PIMs (e.g., use of centrally active antihypertensives and use of amiodarone as first-line antiarrhythmic therapy in supraventricular tachyarrhythmias) and continue to prescribe beneficial CVD medications (e.g., use of beta-blockers in patients with ischaemic heart disease, and ACEIs in patients with systolic heart failure and/or documented coronary artery disease) unless contraindications existed. In fact, (de) prescription practice is determined by several internal and external factors, including prescriber's reluctance to stop medications prescribed by other healthcare providers and a lack of time for comprehensive evaluation of patients.<sup>38</sup> Active involvement of patients and their families in the prescribing decision-making process is an important strategy to empower patients in their self-care,<sup>39</sup> including designing ways to adopt non-pharmacological approaches or substitute with safer alternatives.

While the occurrence of PIMs offers an opportunity to improve care through deprescription, more studies are needed to assess the feasibility of conducting deprescription intervention to reduce PIMs among geriatric rehabilitation inpatients. Moreover, future studies are required to examine the association between the presence of PIMs and PPOs with medication-related hospital admissions, rather than all-cause readmission.

### Strengths and limitations of the study

This is the largest longitudinal study to report on the association between potentially inappropriate prescribing and post-discharge health outcomes in a cohort of geriatric rehabilitation inpatients using STOPP/START v2 criteria. The data were collected through a highly standardized comprehensive assessments performed by a trained multidisciplinary team, providing detailed information, which may strengthen the clinical robustness of our findings. However, it was a single-site study in a geriatric rehabilitation inpatient- the interpretation and generalisability of the findings to other care settings or patients must be done with caution. The observational study design limits the ability to establish a causal relationship between inappropriate medication and clinical outcomes. In addition, whether patients discharged from geriatric rehabilitation were adhered to their medication or have made changes to their prescription following discharge

from geriatric rehabilitation were unable to verify.

## Conclusions

The proportions of patients taking any PIMs and/or PPOs were significantly reduced from acute admission to geriatric rehabilitation discharge. Neither PIM, nor PPO use at geriatric rehabilitation discharge were consistently associated with an increased risk of unplanned readmission and mortality. However, the number of discharge medications were strongly associated with short and long-term readmission. The use and number of PPOs that included vaccine omissions were negatively associated with the longitudinal gains in IADL scores at 90-days following geriatric rehabilitation discharge. Interventions toward patient-tailored appropriate (de) prescribing in geriatric rehabilitation patients are needed, taking the number of medications, unnecessary and omitted medications into account.

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## Author contributions

All authors made substantial contribution to the design and conception of the study. Data collection was performed by CHS and EMR. ABM (first author) and EM involved in data analysis and interpretation of data. The first draft of the manuscript was written by ABM (first author) and all authors reviewed and revised the manuscript. All authors have read and approved the final manuscript.

## Compliance with ethical standards

**Funding:** This study was funded by the Medical Research Future Fund provided by the Melbourne Academic Centre for Health.

**Conflict of interest :** The authors declare that they have no competing interests.

**Ethical approval:** The study was approved by the Melbourne Health Human Research Ethics Committee (HREC/17/MH/103) and performed in accordance with the principles of the Declaration of Helsinki.

**Informed consent:** All participants (or their nominated proxy) provided their written informed consent to participate in this study.

**Data availability :** The RESORT data that support the findings of this study are available from ABM (fifth author) upon reasonable request.

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