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ORIGINAL RESEARCH ARTICLE

Risk factors predictive of adverse drug events and drug-related falls in aged care residents: secondary analysis from the ReMInDAR trial

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Abstract

Background Residents of aged-care facilities have high rates of adverse drug events. This study aimed to identify risk factors for adverse drug events in aged-care residents.

Method This was a secondary study using data from a multicentre randomised controlled trial. Data from 224 residents for whom there was 6 months of baseline information were analysed. We assessed the risk of adverse drug events and falls (post hoc) in the subsequent 6 months. Adverse events were identified via a key word search of the resident care record and adjudicated by a multidisciplinary panel using a modified version of the Naranjo criteria. Covariates identified through univariable logistic regression, including age, sex, medicines, physical activity, cognition (Montreal Cognitive Assessment), previous adverse events and health service use were included in multivariable models.

Results Overall, 224 residents were included, with a mean age of 86 years; 70% were female. 107 (48%) residents had an adverse drug event during the 6-month follow-up. Falls and bleeding were experienced by 73 (33%) and 28 (13%) residents, respectively. Age (odds ratio [OR] 1.05, 95% confidence interval [CI] 1.01–1.10), weight (OR 1.02, 95% CI 1.002–1.04), previous fall (OR 2.58, 95% CI 1.34–4.98) and sedative or hypnotic medicine use (OR 1.98, 95% CI 1.52–2.60) were associated with increased risk of adverse drug events. Increased cognition (OR 0.89, 95% CI 0.83–0.95) was protective. Risk factors for falls were previous fall (OR 3.27, 95% CI 1.68–6.35) and sedative or hypnotic medicines (OR 3.05, 95% CI 1.14–8.16). Increased cognition (OR 0.88, 95% CI 0.83–0.95) was protective.

Conclusion Our results suggest residents with a previous fall, reduced cognition, and prescription of sedative or hypnotic medicines were at higher risk of adverse drug events and should be considered for proactive prevention.

Key Points

Residents of aged-care facilities have high rates of adverse drug events, identifying the risk factors predicting adverse drug events are important to reduce medicine-induced harm in older residents living in aged-care facilities.

Older people living in residential aged-care facilities demonstrating clearly identifiable characteristics, including poor cognition performance, previous fall, increased age or weight, or prescribed sedative or hypnotic agents, should be prioritised for medicines review to consider medicines that can be ceased and to identify changes in symptoms that may indicate deterioration or adverse drug events.

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1 Introduction

Approximately 8% of Australians aged 65 years and over are residents of aged-care facilities [1]. These residents are vulnerable to medication-related harms due to their older age, multimorbidity, frailty, frequent care transitions, polypharmacy, and suboptimal medication use [2–4]. The rate of adverse drug events in aged care ranges from 1 [5] to 27 [6] per 100 resident months. The global estimates of medicine-related harm exceeds over $40 billion every year [7], while more than 40% of medicine-related adverse events are considered preventable [8].

There are several published definitions for medications classified as potentially inappropriate (PIMs) and potentially causing medicine-related harm for elderly adults, including the Beers criteria [9], the Screening Tool of Older Persons' Prescriptions (STOPP), the Screening Tool to Alert to Right Treatment (START) [10], the Drug Utilization Review [11], the Medication Appropriateness Index [12], and the National Committee of Quality Assurance [13]. Among these criteria, the Beers criteria and STOPP criteria are the most commonly referenced. PIMs are recommended to be avoided when treating older people, however due to different continents and different criteria, caution must be exercised when interpreting the observed association between the number of PIMs and negative health outcomes in older adults [14].

Among the PIMs, known high-risk medications (e.g., sedatives and antipsychotic medicines) contribute significantly to adverse drug events in aged-care residents, and are important precipitating factors for falls and acute disease states, as well as contributing to the overall medicine-related burden [15, 16]. In a feasibility trial in aged-care facilities, deprescribing anticholinergic and sedative medicines was associated with significant benefits across a range of important health measures, including mood, frailty, falls and reduced adverse drug events [17].

A novel model of care is necessary within aged-care settings to prevent medication-related harm and improve the quality use of medicines [18]. One potential strategy for preventing adverse drug events is to identify residents who are at higher risk of adverse drug events through formal risk assessment processes so that additional medicine management services can be directed towards this group [19].

We located two prior studies of risk factors, both in the US aged-care setting [8, 20]. The findings from these studies suggest that being a new resident, taking specific medicines, including antibiotics, antipsychotics, or antidepressants, and having comorbidities were all associated with increased risk of adverse drug events [8, 20]. The generalisability of the risk models to other sites is unknown [8, 20].

Risk prediction models for medication-related harms in elderly patients in acute care and community settings are more commonly reported and include the Prediction of Hospitalization due to Adverse Drug Reactions in Elderly Community-Dwelling Patients) score (PADR-EC score) [21], Medicine Risk Score (MERIS) [22], Geriatric Adverse Drug Reaction Score (GerontoNet Score) [23], and Prospective study to develop a model to stratify the RIsk of Medication-related harm in hospitalized Elderly patients (PRIME) [24]. However, none of these risk models were developed or tested in residential aged-care populations.

In 2019, the Australian government announced $25.5 million in funding for aged-care medication management programmes, including more frequent medication reviews to reduce the use of medication to influence resident's behaviour in aged-care settings [25]. Further research is needed to inform the implementation of this policy, including the identification of residents who should be prioritised for follow-up. Identifying independent risk factors for adverse drug events, and validated adverse drug event-focused risk stratification models will enable the aged care staff, general practitioners and pharmacists to consider their residents' risk of medication-related harm as part of routine practice [20]. We aimed to identify independent risk factors for adverse drug events and falls as these events are frequently reported in the aged-care settings.

2 Methods

This study was a secondary post hoc analysis of data from a multicentre randomised controlled trial (ReMInDAR trial) to determine the effectiveness of a 12-month pharmacist service compared with usual care in reducing medicine-induced deterioration, frailty and adverse drug events in older people living in residential aged-care facilities in Australia [26]. Medicine-induced deterioration can be caused by pharmacodynamic effects of medicine or result from the effects of medicines contributing to frailty, cognition, activity or loss of appetite [27–30]. Identification and management of medicine-induced deterioration may support preventing frailty and adverse drug events in older adults [31, 32].

Pharmacists visited residents enrolled in the intervention group every 8 weeks over 12 months, assessing signs and symptoms of medicine-induced deterioration. The pharmacist service included review or care record and medication chart, discussion with resident and care staff, and resident assessment using validated tools. Recommendations concerning medication management were made to the residents' general practitioners.

At enrolment, a total of 248 residents were recruited from 39 residential aged-care facilities across two Australian states (South Australia and Tasmania); data were collected between August 2018 and July 2020. Residents were excluded if they had significant existing frailty, had

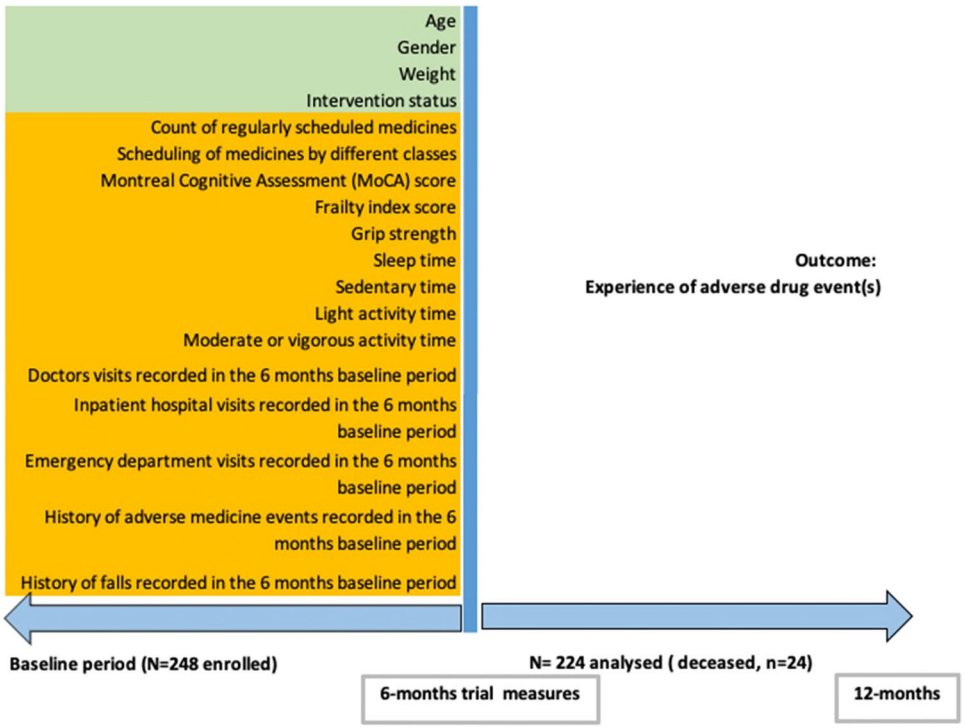

Fig. 1 Variables included in the analysis, by corresponding data collection points

moderate or severe dementia, or were involved in another research project [26]. The median number of beds of participating residential aged-care facilities was 92 (range 29–184). Residents were included if they were using four or more medicines at the time of recruitment or were taking at least one medicine with anticholinergic or sedative properties [26]. At 6 months, 24 residents were deceased, hence in this study, we included a total of 224 residents whose data were available (Fig. 1).

The final months of the ReMInDAR trial (March–July 2020) were affected by global pandemic restrictions due to coronavirus disease 2019 (COVID-19). Although no facilities experienced outbreaks, 53 (9%) pharmacist visits had to be undertaken remotely or were delayed and 35 (6%) were unable to be performed. Twelve-month assessments of 150 (67%) residents were affected.

The study was approved by the Human Research Ethics Committee of the University of South Australia (ID: 0000036440) and the University of Tasmania (ID: H0017022).

2.1 Data Collection

Data collection was based on reviewing residents' health care records and identifying any new-onset illnesses or adverse events present since the last assessment. All residents were assessed by research assistants at baseline and at 6 and 12 months. We used the 6-month trial measure as the baseline point for this study as it provided a 6-month history for identification of risk factors. We then used the 6- to 12-month time period to ascertain the occurrence of the outcome, which was post risk factor identification (see Fig. 1).

2.2 Outcomes

The primary outcome of interest in this study was adverse drug events. We assessed each resident to determine whether they experienced an adverse drug event between 6 and 12 months following their enrolment in the study. Since falls was the most frequent adverse drug event, we conducted a post hoc analysis with fall as the outcome to investigate any difference in risk factors for adverse drug events and falls.

2.3 Assessment of Adverse Drug Events

Adverse events were collected by key word search of the resident care records by research assistants. The key words were predefined as falls (non-injurious and injurious, including fractures), bleeding, bruising, confusion, cough, dizziness, delirium events, urticaria, gastroenteritis, vomiting, nausea, delirium events, bowel or urinary changes, hospitalisation and others. These adverse events were reviewed to assess event type and causality. Initially, the adverse events were independently coded by two research pharmacists (GD, LKE) for causality using the Naranjo algorithm (33). Adverse events were classified as definite (score from 9 to 12), probable (score from 5 to 8), possible (score from 1

to 4), or doubtful (score from 0 to −2) [34]. Classification of the adverse event was submitted to a multidisciplinary panel of clinicians (AA, DR, JW) for confirmation. Of 1978 adverse drug events identified in the 12-month period of the ReMInDAR trial, 30% ($n = 583$) were judged as possible, probable, or definite adverse medicine events [26]. In this analysis, we included 325 adverse drug events that were experienced between baseline and 6 months.

2.4 Independent Variables

A range of physical and cognitive functions that are components of frailty can be affected by medicine use. In older adults, medicines, in particular medicines with sedative and anticholinergic properties, significantly worsen frailty [31]. When compared with the non-frail population, frail older people are more vulnerable to adverse drug events [35]. Evidence suggests that the odds of developing adverse drug events in frail people was double that of non-frail individuals (29% compared with 17%, respectively; odds ratio [OR] 2.1, 95% confidence interval [CI] 1.5–3.0) [36]. In this analysis, we included measurements assessing the variables such as cognition, frailty, physical activities, and hand grip strength, as well as medicines use and doctors' visits. In aged-care facility residents, the Frailty Index (FI) has been shown to have good predictive ability for adverse events [37, 38]. Other risk factors in older people include cognitive impairment [38], physical activity and sedentary behaviour, sleep time [39], and grip strength [40].

2.5 Continuous Variables

Descriptive information of residents, analysed as continuous variables, were age, weight, frailty, physical activity, sedentary behaviour, sleep time, cognition, hand grip strength, count of regularly scheduled medicines, counts of hospitalisations, emergency department visits and doctors visits during the 6-month baseline period.

Frailty was evaluated using the FI [37]; an FI score of ≥0.4 is suggestive of existing significant frailty. The grip strength was measured using a hand-held dynamometer (best of three from the dominant hand) [41]. The physical activities indicating residents' physical activities, including light, moderate-to-vigorous, and moderate intensity, as well as sedentary behaviour (sitting or lying down) and sleep times were assessed using the GENEActive research grade activity tracker [39].

The GENEActive was worn on the wrist by residents for a 7-day period [26]. In older adults, 6–8 h of daily sleep was considered to be within the normal range [42]. Studies assessing physical measurements with GENEActive were reported to range between 538 and 630 min for sedentary activity, 103 and 209 min for light activity, and 134 and 141 min for moderate–vigorous activity in older adults [43].

Cognition was assessed using the Montreal Cognitive Assessment (MoCA) test [44], which has a score between 0 and 30, with a higher score indicating better cognition. A score of ≤17 indicates dementia [44]. Medicine use was collected from the facility-maintained medication chart by independent research assistants, and health service use was based on hospital, emergency and doctors' claims data.

2.6 Categorical Variables

Covariates included sex, intervention status, and previous adverse drug events and falls recorded in the first 6 months of the trial. Furthermore, use of any medicines within each of the following medicine classes were analysed: Alzheimer disease treatments, antibiotics or anti-infectives, anticholinergics, anti-gout medicines, antihistamines, antihyperlipidemics, antineoplastics, antiparkinsonians, antipsychotics, antiseizure medicines, antithrombotics (anticoagulants and antiplatelets), antihypertensives, diuretics, gastrointestinal medicines, hypoglycemics, muscle relaxants, opioid and non-opioid analgesics, antidepressants, nutrients or supplements, osteoporosis medicines, sedatives and hypnotics, and thyroid medicines.

Inpatient hospitalisations, emergency department visits and doctors' visits in the 6 months prior were calculated using the hospital records as well as Medicare Benefit Schedule (MBS) claims. The MBS contains a list of health professional services subsidised by the Australian Government for a wide range of health services, including consultations, diagnostic tests and operations [45].

A binary variable indicating residents whose 12-month assessments were affected by COVID-19 access restrictions was also considered for inclusion as a covariate.

2.7 Statistical Analysis

Participant characteristics are presented as descriptive statistics: mean (standard deviation [SD]), median (interquartile range [IQR]) or count (percent [%]), as appropriate.

Specific medicines and total count were analysed at the level of unique medicine, classified using the Anatomical Therapeutic and Chemical codes (46). See electronic supplementary material [ESM] Table S1 for medicines with sedative and hypnotic properties that were assessed in the study.

For both binary outcomes, univariable logistic regression modelled each risk factor separately. Variables with a p-value < 0.1 were included in a multivariable model, as well as intervention status. Variables considered for selection included age, weight, frailty, physical activity, cognition, hand grip strength, count of regularly scheduled

medicines, specific medicines, counts of hospitalisations, emergency department visits and doctors' visits, adverse drug events occurring during the 6-month baseline period, and whether 12-month assessments were affected by COVID-19 restrictions. Linearity of continuous variables was assessed graphically.

There were missing data for 12 residents who refused or were unable to complete the MoCA assessment at 6 months and there were two residents where specific medicine information was unavailable. Eleven residents had missing data for weight at 6 months. Multiple imputation with chained equations for missing data was performed using the R package 'mice' [47]. One hundred iterations were used and estimates combined using Rubin's rules [48]. Binary data were imputed using logistic regression and weight with linear regression. Since cognition was limited to 0–30, predictive mean matching was used, which has been found to produce adequate association estimates for bounded variables [49]. In the final multivariable model, covariates and interactions were retained if $p < 0.1$.

Results are presented as ORs and 95% CIs. Analyses were performed using R Version 4.2.1 (R Foundation for Statistical Computing, Vienna Austria) [50].

2.7.1 Model Performance

The predictive discrimination of the optimum models for adverse drug events were assessed using the concordance statistic (C-statistic). The predictive discrimination refers to the ability of a model to clearly distinguish between the two binary outcome categories; a value of C-statistic above 0.7 is considered acceptable [51]. The pooled C-statistic was calculated using the R package 'miceafter'.

We tested the multicollinearity of the variables and the strength of the correlation by estimating the variance inflation factors (VIFs), with a VIF < 5 considered to indicate no collinearity [52].

3 Results

The characteristics of 224 residents measured at the 6-month timepoint are shown in Table 1. The mean age of residents was 86 years (SD 8) and 70 (31%) were male.

In the 6-month baseline period, 165 (74%) residents had claims for doctors visits, 26 (12%) residents had an inpatient hospitalisation, and 29 (13%) participants had an emergency department visit (median 1, IQR 0–2). Ninety (40%) residents had a history of adverse drug events and 60 (27%) had a previous fall. The median number of regularly scheduled medicines was 11 (IQR 8–14), with 184 (83%) residents prescribed sedative or hypnotic medicines. Frequencies of other prescribed medicines are reported in ESM Table S2. The median MoCA score was 22 (IQR 18–25). Mean sleep time was 8.9 h (SD 1.1), which is higher than the normal range in older adults of 6–8 h.

3.1 Frequency and Type of Adverse Drug Events

Almost half of all residents had at least one adverse drug event between 6 and 12 months ($n = 107$, 48%). Falls were the most frequent event, experienced by 73 (33%) residents, followed by bleeding reported in 28 (13%) residents (Table 2). Bleeding was most likely attributed to the use of antithrombotic medicines (anticoagulants and antiplatelets).

3.2 Risk Factors

Factors independently associated with a higher risk of having an adverse drug event included age (OR 1.05, 95% CI 1.01–1.10), weight (OR 1.02, 95% CI 1.002–1.04), previous fall (OR 2.58, 95% CI 1.34–4.98) and prescribing of sedative or hypnotic medicines (OR 2.25, 95% CI 1.01–5.00) [Table 3]. A higher MoCA score was protective (OR 0.89, 95% CI 0.83–0.95). The model had a moderate predictive power, with C-statistic equal to 0.73 (0.66–0.79). No collinearity was detected (VIF <5 for all variables). There were no significant interactions.

For falls, the risk was higher when a resident had had a previous fall (OR 3.27, 95% CI 1.68–6.35) or used sedative or hypnotic medicines (OR 3.05, 95% CI 1.14–8.16) [Table 4]. Increased MoCA score was protective (OR 0.88, 95% CI 0.83–0.95). The model for falls showed moderate power (C-statistic = 0.75, 0.67–0.81), no collinearity was identified, and no interactions were significant. All covariates identified in univariable analysis are shown in ESM Tables S3 and S4.

4 Discussion

We found previous falls, lower cognition scores, and sedative and hypnotic medicine use were predictive of both future adverse drug events and falls in residents. In addition, age and weight increased the risk of adverse drug events. The risk factors reported in our study are possible to identify during clinical reviews and thus could be used for prioritising residents at risk of harm from medicines.

The predictors we identified are supported by other research. Sedative and hypnotic medicines are well recognised as a cause of adverse drug events. A case-control nested study assessed the risk factors for adverse events among US residents. Adverse drug events were identified in 410 nursing home residents and independent risk factors

Table 1 Principal characteristics of the study population at 6 months

Characteristic [$N = 224$][a]	
Age, years [mean (SD)]	86 (8)
Intervention group [*n* (%)]	105 (47)
Weight, kg [mean (SD)]	74 (18)
Male sex [*n* (%)]	70 (31)
Number of regularly scheduled medicines [median (IQR)]	11 (8–14)
Use of sedative or hypnotic medicines ($N = 222$) [*n* (%)]	184 (83)
Frailty Index [mean (SD)]	0.29 (0.1)
Highest grip strength ($N = 208$) [mean (SD)]	17.6 (7.7)
MoCA score ($N = 212$) [median (IQR)]	22 (18–25)
Sedentary time, hours ($N = 122$) [mean (SD)]	12.6 (1.5)
Sleep time/in bed, hours ($N = 122$) [mean (SD)]	8.9 (1.1)
Light activity time, hours ($N = 122$) [median (IQR)]	1.5 (0.9–2.2)
Moderate and vigorous activity time, hours ($N = 122$) [median (IQR)]	0.5 (0.2–1.1)
Any visit to emergency department [*n* (%)]	29 (13)
Number of visits to the emergency department [median (IQR)]	1 (0–2)
Any hospital admission [*n* (%)]	26 (12)
Number of hospital admissions [median (IQR)]	1 (0–4)
Any outpatient hospital care [*n* (%)]	165 (74)
Number of outpatient care episodes [median (IQR)]	12 (0–22)
Previous adverse drug event (baseline–6 months) [*n* (%)]	90 (40)
Previous fall (baseline–6 months) [*n* (%)]	60 (27)
Affected by COVID-19 lockdowns [*n* (%)]	150 (67)

SD standard deviation, *IQR* interquartile range, *MoCA* Montreal Cognitive Assessment, *COVID-19* coronavirus disease 2019

[a]Unless indicated otherwise

Table 2 Classification of adverse drug events

Type of adverse medicine events	Number of residents ($n = 107$)	Number of adverse drug events ($n = 325$)
Fall	73	191
Bleeding (any)	28	53
Bruising	17	30
Dizziness	15	18
Confusion	4	14
Constipation	4	4
Urticaria (rash)	3	4
Cough	2	2
Gastroenteritis, vomiting, nausea	3	3
Faecal impaction	1	1
Other[a]	4	5

[a]Includes skin tear, spontaneous eye bleeding, red eye with discharge

identified were schedule of sedatives and hypnotics (cases, 33.4% vs. controls, 23.7%; $p < 0.01$) [20].

Table 3 Multivariable logistic regression of risk factors for having any adverse drug event

Variable	OR (95% CI)	*p*-Value
Group: Intervention	1.28 (0.71–2.32)	0.41
Age[a]	1.05 (1.01–1.10)	0.018
Weight, kg	1.02 (1.002–1.04)	0.028
MoCA[b]	0.89 (0.83–0.95)	<0.001
Previous fall	2.58 (1.34–4.98)	0.005
Sedatives or hypnotics	2.25 (1.01–5.00)	0.047

OR odds ratio, *CI* confidence interval, *MoCA* Montreal Cognitive Assessment

[a]Every year increase

[b]Every point increase

A 2008 literature review assessing medicine-induced errors in acute care settings also reported that sedative medicines were the medicines commonly implicated [53].

We found increased cognition to be protective against adverse drug events. Similar findings were reported in systematic reviews (54, 55), with poorer cognitive performance

Table 4 Multivariable logistic regression of risk factors for having a fall

Variable	OR (95% CI)	*p*-Value
Group: intervention	0.86 (0.46–1.62)	0.64
Weight, kg	1.02 (0.999–1.03)	0.07
MoCA[a]	0.88 (0.83–0.95)	<0.001
Previous fall	3.27 (1.68–6.35)	<0.001
Sedatives or hypnotics	3.05 (1.14–8.16)	0.03

OR odds ratio, *CI* confidence interval, *MoCA* Montreal Cognitive Assessment

[a]Every point increase

significantly associated with higher mortality rates, dementia, decreased activity, hospitalisation and reduced quality of life [54, 55]. We did not locate any studies assessing the association between the risk of adverse events and cognition when measured using the MoCA. For this reason, direct comparison of our results with other studies is difficult; however, our findings reinforce the need to prioritise residents with cognitive impairment.

Previous studies have shown frailty is associated with adverse drug events (31, 35). In our study, frailty was measured using the FI and was not observed to be an independent predictor, which may be due to the fact that non-frail residents were enrolled in our study.

Increasing age is a significant contributing factor to ADR for adverse drug events in older residents [56]. In our study, with every additional year, residents are at a 5% higher risk of having an adverse drug event (OR 1.05, 95% CI 1.01–1.10; $p = 0.018$). No comparable findings were reported in other studies. Furthermore, a significantly associated risk factor for adverse drug events was the weight of residents in our study. The mean baseline body weight was 74 kg, suggesting that our findings could be validated in another sample.

Falls are frequent in aged care, with estimates that one in two Australian residents living in aged care fall within a 6-month period [15]; a previous fall is also recognised as one of the strongest predictors of falls [57]. A systematic review analysing the risk factors for falls included 15 studies performed in aged-care residents (mean age 80 years) [58]. Overall, the association with a previous fall was threefold (OR 3.06, 95% CI 2.12–4.41), which was confirmed in our study [58].

We found using medicines with sedative and hypnotic properties was an independent factor for falls. A meta-analysis of the impact of nine medication classes on falls in older residents assessed the association between falls and sedative hypnotics, and found the risk of falling was lower than our findings (OR 1.47, 95% CI 1.35–1.62) [59]. Further support for our results comes from a previous systematic review assessing the evidence linking drugs with falls in older people. The risk for falls was higher in those prescribed sedatives and hypnotic medicines (OR 1.54, 95% CI 1.40–1.70) [60].

In our study, the count of prescribed medicines was not found to be a predictor for adverse drug events. The association between risk of having an adverse outcome and polypharmacy in the aged-care population is not universally confirmed in the literature [61, 62]. In aged-care settings, almost 50% of the population is exposed to five or more medicines [61]. This may indicate that the type of medicines used have a more important impact on risk for experiencing adverse drug events rather than the count of medicines.

4.1 Strengths and Limitations

To our knowledge, this is the first study to identify risk factors associated with adverse drug events in older residents living in aged-care facilities, where data were collected longitudinally. Longitudinal measurements pertaining to older residents' cognitive and physical function, as well their medicine use, were objectively collected by the ReMInDAR staff, who received training on using validated scales such as the GENEActiv activity tracker [39] and MoCA prior to engaging in the trial [26, 37, 41, 44]. Data on inpatient and outpatient hospitalisations, as well as emergency visits, were comprehensive, as they were obtained employing the claims from health service use.

The analysis did not specifically focus on PIMs because this required an extra decision-making process. In order to detect specific medicines, we included all medicine classes, without limiting to PIMs only.

The model fit was evaluated using the C-statistic; all models indicated a good fit with a C-statistic > 0.7. However, a limitation of our results is that the models were not tested in another sample. Further studies may be required to validate the risk factors.

The ReMInDAR trial enrolled residents who were not frail and not cognitively impaired, thus caution must be exercised when generalising the results to a frailer aged-care population.

During the final months of the trial, which were affected by COVID-19 restrictions, some problems and adverse drug events may have been underreported. However, our analysis indicated that COVID-19 restrictions were not a risk factor for adverse drug events in this study.

5 Conclusion

We aimed to identify resident-level independent factors predicting risk of adverse drug events, with the ultimate goal to better recognise residents most at risk, to support interventions to provide better care. In residential aged-care facilities, medicines are often prescribed long-term. Pharmacists and aged-care staff play an important role in monitoring residents. Aged-care residents who demonstrate clearly identifiable characteristics, including poor cognition performance on MoCA, previous fall, and prescribed sedative or hypnotic agents, should be prioritised for pharmacists to perform medicine reviews. Upon identifying the PIMs, recommendations should be provided to discontinue the medicines. Furthermore, clinicians should identify and monitor changes in signs and symptoms that may indicate deterioration or adverse drug events in aged-care residents.

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Declarations

Authors' contributions As principal investigator, ER had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Conception and design: ER, GD, NPN, LB, NP, TLK. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: GD, ER, NPN, TLK. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: GD, NPN, ER, NP, TLK. Obtained funding: ER, DR, LKE, LB, NP, Parfitt, JW, RL. Administrative, technical, or material support: GD, ER, RLB, NP, TLK, AA, RL. Supervision: ER

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Code and data availability De-identified data and codes can be requested from the corresponding author.

Conflicts of interests Gereltuya Dorj, Nibu Parameswaran Nair, Luke Bereznicki, Thu-Lan Kelly, Nicole Pratt, Lisa Kalisch-Ellet, Andre Andrade, Debra Rowett, Joseph Whitehouse, Rebecca L. Bilton, Renly Lim, Imaina Widagdo and Elizabeth Roughead have no conflicts of interest to declare.

Ethical approval This study was approved by the Human Research Ethics Committee of the University of South Australia (ID: 0000036440) and the University of Tasmania (ID: H0017022).

Consent to participate Not applicable.

Consent for publication Not applicable.

Informed consent Not required for publication.

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