Pharmaceutical Society of Australia Ltd.

FEBRUARY 2020

MEDICINE SAFETY: **AGED CARE**

ABOUT PSA

PSA is the only Australian Government-recognised peak national professional pharmacy organisation representing all of Australia's 32,000 pharmacists working in all sectors and across all locations. PSA is committed to supporting pharmacists in helping Australians to access quality, safe, equitable, efficient and effective healthcare.

PSA believes the expertise of pharmacists can be better utilised to address the health care needs of all Australians. PSA works to identify, unlock and advance opportunities for pharmacists to realise their full potential, to be appropriately recognised and fairly remunerated.

PSA has a strong and engaged membership base that provides high-quality health care and are the custodians for safe and effective medicine use for the Australian community. PSA leads and supports innovative and evidence-based healthcare service delivery by pharmacists.

PSA provides high-quality practitioner development and practice support to pharmacists and is the custodian of the professional practice standards and guidelines to ensure quality and integrity in the practice of pharmacy.

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ACKNOWLEDGEMENTS

PSA thanks the staff of Donwood Community Aged Care facility (Croydon, Victoria), Chemist Discount Centre Boronia (Victoria), consultant pharmacist Neil Petrie MPS and community pharmacist Rebecca Barron MPS for their participation in photography. Photography by Damien Pleming and Gareth Allsopp.

PSA also aknowledges the contribution of Associate Professor Chris Freeman, Dr Shane Jackson, Monika Boogs, Peter Guthrey and Rhyan Stanley.

Design: Mahlab

Suggested citation: Pharmaceutical Society of Australia. Medicine safety: aged care. Canberra: PSA; 2020.

PSA gratefully acknowledges the financial contribution of PDL for the development of the original report, *Medicine Safety: Take Care* (2019), as well as ongoing support for PSA's annual reports on medicine safety.

ISBN
Print: 978-0-908185-30-6
Online: 978-0-908185-31-3

PSA FOREWORD

The Pharmaceutical Society of Australia commissioned the Quality Use of Medicines and Pharmacy Research Centre at the University of South Australia, led by Professor Libby Roughead to provide a report on the extent of medicine harms within the aged care setting. This current report, following on from PSA's *Medicine Safety: Take Care* report, provides sobering data about the real and current problems afflicting our aged care residents across Australia.

The data is clear. The current system is failing and new approaches are needed to improve medicine use in aged care.

Twenty per cent of unplanned hospital admissions for aged care residents are a result of inappropriate medicine use. This is a game of Russian roulette, and unfortunately our older Australians are paying the price with either their life or their quality of life.

Nearly all of our aged care residents in Australia have at least one medicine-related problem. Starkly, most have three or more problems, including dangerous and life-threatening drug interactions, and medicine dosage problems including overdosing.

Half of all our residents are taking medicines that cause sedation or confusion, with twenty per cent taking antipsychotics and more than half of these residents are taking the medicines for far too long.

We need to do more for our older Australians living in residential aged care and those supported at home. Medicines are developed, prescribed and dispensed for supporting good health and to keep people well. In a large number of circumstances for older Australians, the opposite is happening. Now is the time to do more for residents of aged care in Australia. To provide a safe environment that minimises medicine harm and maximises the role of pharmacists as the stewards of medicine safety to prevent this harm from occurring.

The Australian Government must respond with appropriate support including funding and structural reform to keep older Australians safe, and receiving the best possible care.

Pharmacists are the key to this and we look forward to working with the Government, the aged care sector, other healthcare professionals, residents and families to improve the current situation – which can no longer be tolerated.

Associate Professor Chris Freeman
National President

EXECUTIVE SUMMARY

EXTENT OF PROBLEM

Medicine-related problems

- Over 95% of people living in aged care facilities have at least one problem with their medicines detected at the time of a medicines review; most have three problems.
- One in six medicine-related problems are due to adverse medicine reactions.
- 6% of people living in aged care were administered at least one potentially hazardous medicine combination.

Inappropriate medicine use

- Over half of all people living in aged care facilities are prescribed medicines that are considered potentially inappropriate in older people.
- One in five unplanned hospital admissions among people living in aged care facilities are a result of taking medicines generally considered potentially inappropriate for older people.
- 40% to 50% of people living in aged care are on medicines that have the potential to cause sedation or confusion.
- 50% of people with dementia are taking medicines with anticholinergic properties, which can worsen confusion and other symptoms of dementia
- One-fifth of people living in aged care are on antipsychotics; more than half use the medicine for too long.
- Up to one-third of people living in aged care are taking benzodiazepines; more than half use the medicine for too long.
- Half to three-quarters of people on proton pump inhibitors use the medicine for too long.

Administration errors

- Up to one-third of people living in aged care facilities have their medicines altered; 15% to 32% of the medicines should not have been altered.

PRELUDE

Older Australians often suffer from multiple chronic illnesses and therefore use many medicines.[1] In the aged care setting, there are high rates of medicine use by older people, with, on average, individuals using between 9 and 11 different medicines.[2,3] As the number of medicines that a person takes increases, the number of medicine-related problems that a person experience also increases. Problems with medicine use become particularly challenging when we get older. Changes to the body systems make older people more sensitive to the effects of the medicines they take. This means older people are at increased risk of adverse events, medicine-medicine interactions and medicine-disease interactions.

In this *Medicine Safety: Aged Care* report, we examine the literature that looked into the problems with medicine use in residential aged care facilities in Australia. We collate findings from different sources of information (refer **Appendix 1**) to provide a comprehensive picture on the extent and types of medicine-related problems in aged care in Australia.

MEDICINE-RELATED PROBLEMS IN AGED CARE

Over 95% of people living in aged care facilities have at least one problem with their medicines *detected* at the time of a medicines review; most have three problems.

There are significant benefits for older people with multiple conditions to be taking medicines, if the benefits for taking the medicines outweigh the risks. Many times, however, older people may be taking medicines that are either not helping their condition, are no longer needed or cause unwanted side effects or harmful interactions.

There are many types of medicine-related problems which can increase risk of patient harm. Taking many medicines increases the risk of errors such as the wrong medicine being given. Some medicines interact with other medicines causing serious problems. Where combination products containing two or more medicines are prescribed, there is a possibility of duplicate medicine use if existing medicines are not ceased. Some medicines that are prescribed may not be appropriate, or the dose selected may be too high or too low. In this section we look at the extent of the problem and the types of medicine-related problems among people living in residential aged care facilities.

Australian studies show that at the time a medicines review is undertaken almost all older adults in aged care facilities have at least one medicine-related problem (**Figure 1**), with an average of three problems per person (**Figure 2**).[4-7]

Figure 1: Prevalence of medicine-related problems identified in Residential Medication Management Reviews.

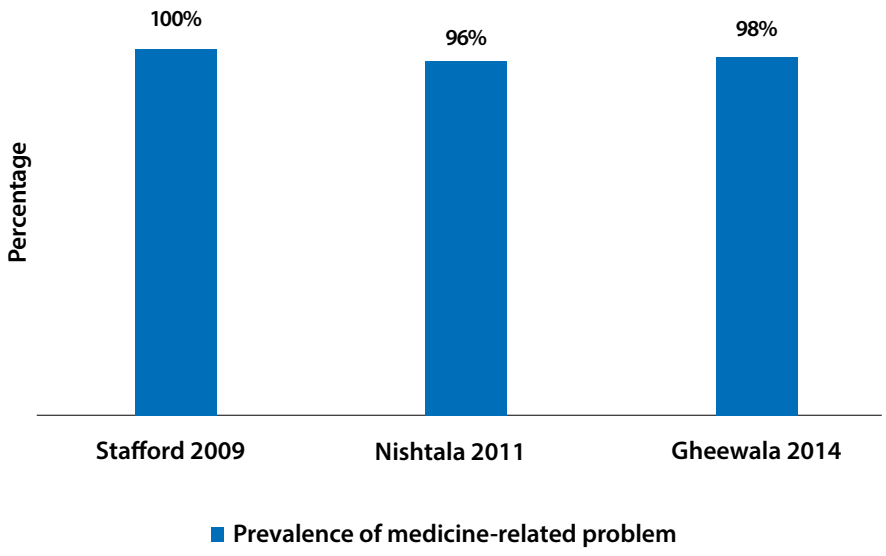
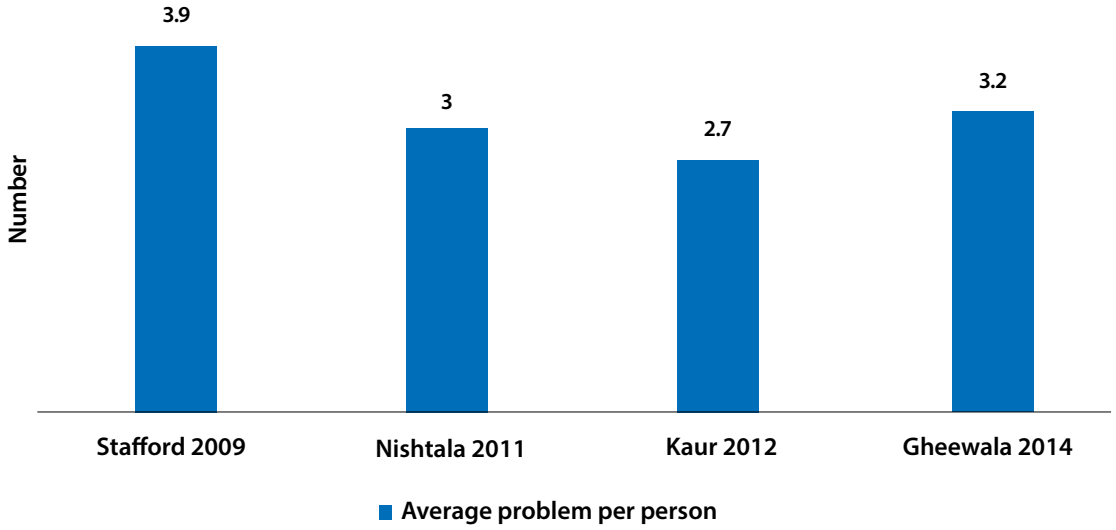


Figure 2: Average number of medicine-related problems per person identified in Residential Medication Management Reviews.

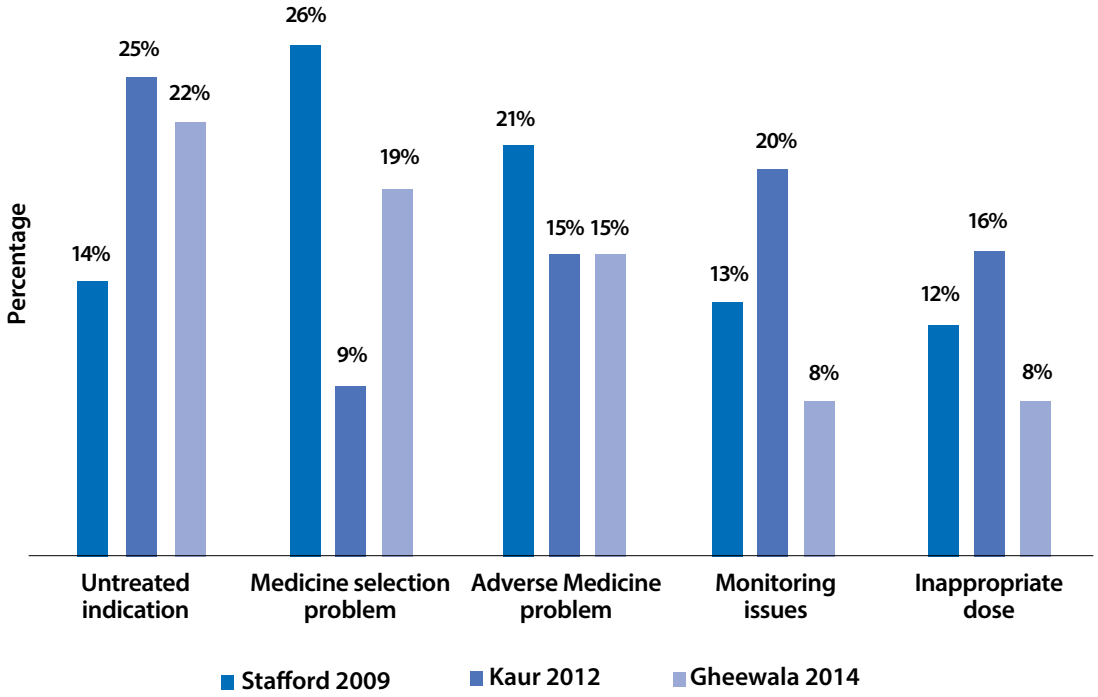


The most common types of medicine-related problems that were identified in the aged care setting include not receiving a needed medicine, use of an inappropriate medicine, an adverse medicine reaction, lack of laboratory monitoring and use of an inappropriate dose (**Figure 3, Appendix 2**).

About one in five medicine-related problems were attributed to people living in aged care facilities not receiving a needed medicine, one in five problems due to an inappropriate medicine selection, and one in six problems attributed to adverse medicine reactions. All the studies assessing the prevalence of medicine-related problems in aged care have reported the types of problems as a percentage of all problems. Reporting results as the percentage of all problems is not the same thing as reporting the percentage of people who have the problem. To estimate the percentage of people who have the problem, we examined Australian studies identifying medicine-related problems in older people living in the community.[8-14] Similarly to the studies of people living in aged care, the studies assessing medicine-related problems in older people living in the community also found that one in six problems were attributed to an adverse medicine reaction.

Three studies in the community reported the results as the percentage of people who had an adverse medicine reaction. Two studies found that one in five people had an adverse medicine reaction at the time of a medicines review[11,15] and the third study found one in four people attending a memory clinic or aged care clinic was suffering an adverse medicine reaction.[16] Given the similarity of results of the proportion of medicine-related problems that are attributed to adverse reactions across aged care and community studies, it is also likely that the one in five persons living in aged care were experiencing an adverse medicine reaction at the time of the medicines review.

Figure 3: Common types of medicine-related problems (as a percentage of all problems) identified in Residential Medication Management Reviews.



It must be remembered that while we report percentages, it is real people who are suffering the consequences of adverse reactions as the case study in **Box 1** shows.

Box 1: Case study

Adverse medicine reactions

A 70-year-old woman was referred to her pharmacist by her doctor for a medicines review because she had increased difficulty in swallowing and her health had declined. The woman was on eight regular medicines and five "as required" medicines. The medicine, risperidone has been recently added to her medicine regimen to manage behavioural and psychological symptoms of dementia (BPSD). The woman could not swallow her medicines, had increased blood pressure, high temperature, fast heart rate, and increasing drowsiness and confusion. The pharmacist suspected this might be due to an adverse medicine reaction, risperidone-induced neuroleptic malignant syndrome, and contacted the doctor immediately. The doctor ordered cessation of the risperidone (and oxazepam to reduce the medication burden). Following cessation of risperidone, the woman's temperature returned to normal, she started eating normally, had no difficulties swallowing and became more mobile.

***Source**: Morcos et al 2018*[17]

6%

of people living in aged care were administered at least one potentially hazardous medicine combination.

When people take multiple medicines it is interactions between the medicines that can be responsible for the harms. We identified two additional studies that reported the prevalence of medicine interactions among people living in aged care.[18,19] A Sydney study involving 3,876 people living in aged care examined hazardous medicine interactions; those that are likely to be harmful. It found that 6% of people were administered at least one potentially hazardous medicine combination. Another study, involving 317 people with dementia living in aged care in Queensland, used a different method and examined all medicine-medicine interactions that occurred (including less hazardous interactions). It found that 41% of people living in aged care facilities had at least one potential medicine-medicine interaction. Because multiple medicine use is common, people can have more than one medicine-medicine interaction occurring at the same time.

In this study there were 200 medicine-medicine interactions found among the 130 people with at least one interaction identified, meaning most people had more than one interaction identified. The proportion of interactions that were identified as severe was reported as a percentage of interactions, not people, with the findings showing that two in every five medicine interactions were considered potentially severe interactions.[19]

Box 2: Case study

Medicine interaction

One medicine interaction, known as the "triple whammy" is an interaction involving three types of medicines; non-steroidal anti-inflammatory medicines (an analgesic), with diuretics and medicines for high blood pressure that affect a body system known as the renin-angiotensin system. This interaction is of concern as it increases the risk of acute kidney failure.[20] A study involving 10,367 older people living in aged care facilities in New South Wales and the Australian Capital Territory found this potentially hazardous interaction was prescribed for 1.7% of people.[21]

Box 3: Case study

Medicine interaction

An 82-year-old man living in an aged care facility had a fall and extensive bruising on his back, buttocks and thighs and was admitted to the hospital. The man was on **warfarin 12 mg** daily, a medicine to prevent blood clots. The man had been on medicines for tuberculosis, including **rifampicin**, which interacts with warfarin and means the warfarin dose has to be increased. Prior to starting rifampicin, the man was on warfarin 4 mg daily, however, on ceasing the rifampicin, the dose of warfarin was not reduced to 4 mg but remained at 12 mg. This meant the man was getting too much warfarin, which caused the extensive bruising.

The doctors and pharmacists determined that the initial medicine-medicine interaction between warfarin and rifampicin was the reason the dose of warfarin was now too high. Warfarin 4 mg daily was safely re-initiated five days after hospital admission. Following the incident, the pharmacy department of the hospital started an education process to increase knowledge among clinicians about rifampicin-warfarin interaction.

Comment: This case study emphasises the importance of awareness of medicine-medicine interactions at any time when medicines are being used. Failure to identify the interactions and the need modify the dose can result in significant patient harm.

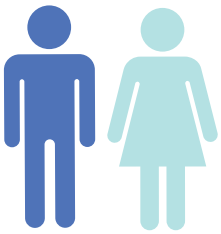
Source: *Tong et al 2014*[22]

Another way of determining whether there are problems with medicine use is using a validated tool called the medication appropriateness index.[23] The medication appropriateness index consists of 10 criteria assessing the reason for use of the medicine, whether the medicine is being effective, the appropriateness of the dosage, the accuracy and practicality of the directions for use, the presence of medicine interactions, the presence of medicine-disease interactions, the cost of the medicines compared to alternatives, the appropriateness of the duration and whether any medicines have been duplicated. Each criterion is given a rating between 1 and 3; a higher rating indicates a higher degree of inappropriateness. A Sydney study involving 223 people living in aged care used this method to investigate medication use appropriateness and found that all people had at least one inappropriate rating.[24] This result is consistent with the findings from the studies assessing medicine-related problems, which showed that nearly all people living in aged care had at least one problem at the time of their medicines review.

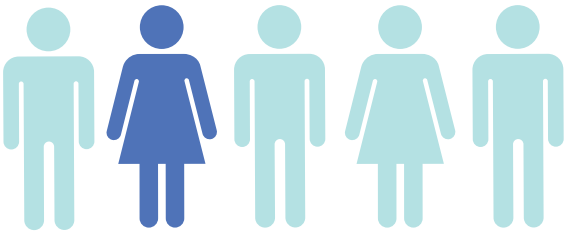
Collectively, these results show that medicine-related problems frequently occur in aged care facilities, with all people who take medicines affected. The types of problems include problems that cause harm, such as the finding that one in five persons is likely to be suffering an adverse reaction from their medicines. It should be noted that under-treatment is also commonly identified as a problem, with one in five problems being related to lack of needed medicines. The 2019 Royal Commission into Aged Care Quality and Safety Interim Report[25] highlighted that problems with medicine use among people living in aged care facilities are a frequent cause of concern; one third of issues raised in the online submissions to the Royal Commission were related to problems with medicine management in aged care.[25]

INAPPROPRIATE MEDICINE USE

In the previous section, the studies assessing the extent of medicine-related problems in aged care reported that one in five medicine problems were due to inappropriate selection of medicines. We can gain more insight into the type of inappropriate medicine use in aged care by examining studies that have focused on problems with specific types of medicines. Medicines can be considered inappropriate in older people for a number of reasons. With some medicines, the risk-benefit profile changes according to age. Because of age-related changes in the body, older people are more sensitive to medicines and medicines often take longer to clear from their body. For these reasons, medicines that might be considered beneficial in younger people are considered less beneficial and sometimes harmful in older people. The duration of use of a medicine is also considered a factor in determining whether medicines are considered appropriate. For some medicines, the benefit to harm ratio is considered reasonable for short term use, but not with long term use because the risk of harms is extended over time. Medicines can also be considered inappropriate when more effective or safer alternatives are available.



More than half of all people living in aged care facilities are prescribed medicines that are considered potentially inappropriate in older people.



Almost one in five unplanned hospital admissions among people living in aged care facilities are a result of taking medicines considered potentially inappropriate for older people.

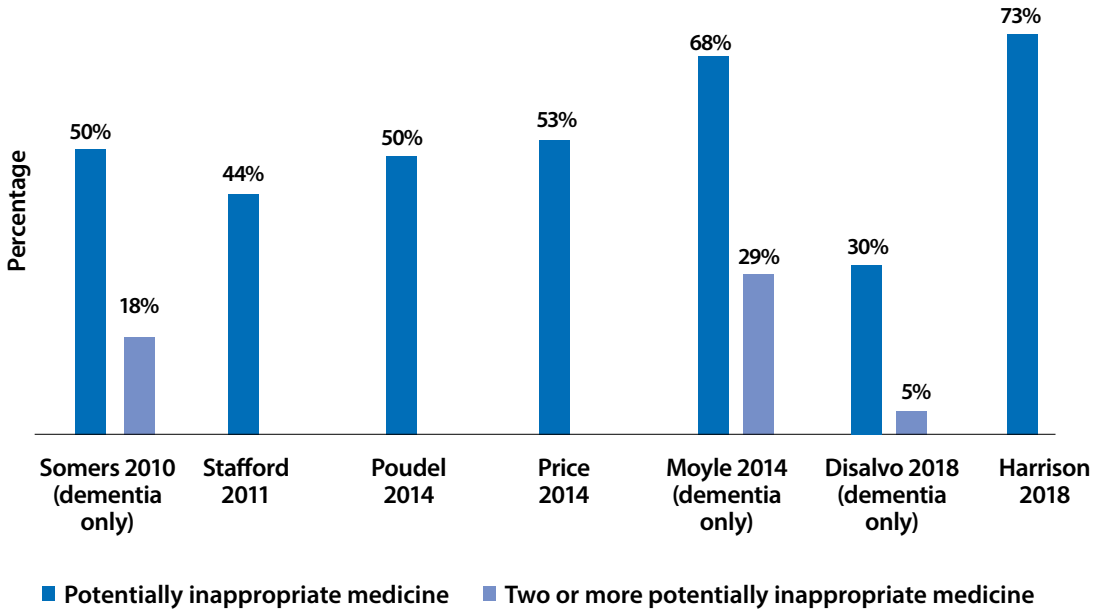
MEDICINES CONSIDERED POTENTIALLY INAPPROPRIATE IN OLDER PEOPLE: GUIDELINE DEFINED

Many guidelines have been developed by doctors and pharmacists who specialise in aged care identifying medicines considered potentially inappropriate in older people. The guidelines commonly cited in the academic literature include the Beers Criteria,[26-28] the STOPP/START criteria,[29] McLeod's criteria[30] and Palliative Excellence in Alzheimer Care Efforts (PEACE) criteria.[31] All these guidelines list medicines considered potentially inappropriate to use in the older people. The use of the word "potentially" is deliberate as there may be some individual cases where the medicine is the only option available for some people. While we might expect some older people to be on the medicines listed as potentially inappropriate, we would not expect the majority of older Australians to be on these medicines.

There have been seven Australian studies that have used these guidelines to examine the extent of use of potentially inappropriate medicines in people living in aged care facilities. The studies found that between 30% and 73% of people living in aged care were prescribed at least one potentially inappropriate medicine (**Figure 4**). Five studies[19,32-35] defined potentially inappropriate medicines using the Beers Criteria, one study used both the Beers criteria and the McLeod's criteria[36] and one study used the PEACE criteria.[37]

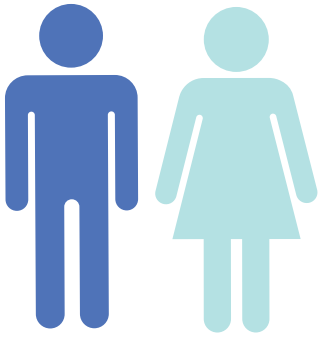
The use of potentially inappropriate medicines by older people has been associated with increased risk of harm. A Western Australian study involving almost 250,000 older people used health claims data to assess the risk of unplanned hospital admissions in people using potentially inappropriate medicines between 1993 and 2005.[32] The study found that 18% of unplanned hospital admissions among people living in aged care was due to the potentially inappropriate medicine. This study also showed that if people took more than one potentially inappropriate medicines concurrently, then the risk of unplanned hospital admission rose even further. This study did not identify the reasons for hospital admission. However, another Australian study undertaken in older people reported that the types of hospital admissions due to potentially inappropriate medicine use included falls, heart failure, confusion, constipation, and gastro-intestinal bleed. This population included all older people, not just people living in aged care.[38]

Figure 4: Percentage of people living in aged care facilities in Australia taking potentially inappropriate medicine.



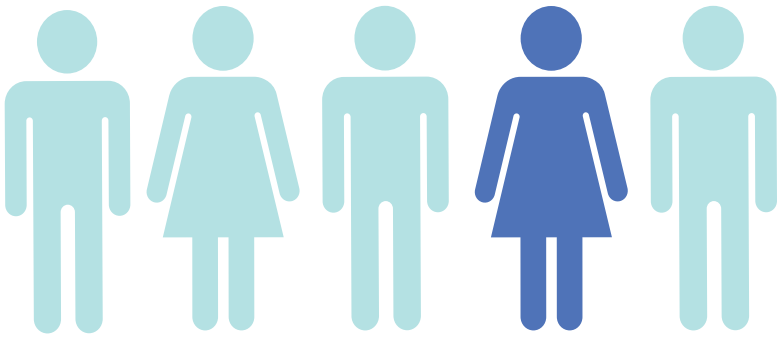
Note: Disalvo 2018 used the PEACE criteria which included only a limited number of medicines, which explains the lower prevalence of potentially inappropriate medicine use.

MEDICINES CONSIDERED INAPPROPRIATE IN OLDER PEOPLE BECAUSE OF SIDE EFFECTS



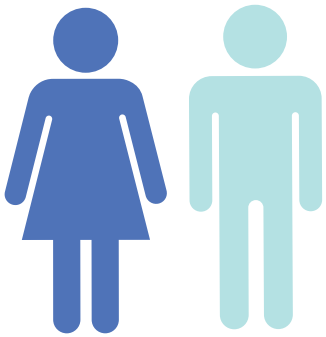
Up to half of all people living in aged care are on medicines that have the potential to cause sedation or confusion.

Some medicines are considered inappropriate in older people because of their side effects and the guidelines identifying potentially inappropriate medicine use in older people include many medicines for this reason. The side effects of medicines that are considered particularly problematic in older people are sedation and confusion. Both of these side effects can contribute to a person's overall functional decline[39-42] and increase the risk of a person having a fall,[39-42] or developing delirium.[43-45] Many medicines that have the side effects of sedation or confusion are in the group of medicines collectively known as psychotropic medicines. For some medicines, the side effect is directly related to its intended action; for example, the medicine is designed to cause sedation, but too high a dose may lead to over-sedation. For other medicines, the side effect is due to the indirect action of the medicine; for example, the medicine may be used for pain but may also cause sedation or confusion. Additional problems can arise when medicines with the same types of side effects are used together. For example, when two medicines that both have the side effect of drowsiness are used together, the effects can be additive.[46]



One in five people living in aged care are taking two or more medicines that have the potential to cause sedation or confusion.

Medicines with anticholinergic properties



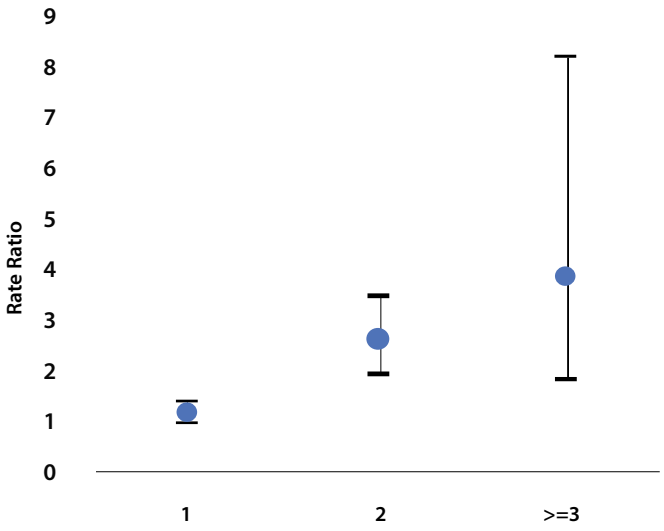
Half of all people living in aged care are taking medicines that have anticholinergic properties; these medicines can contribute to cognitive impairment or confusion.

A particular group of medicines which are not recommended for use in older people because they can contribute to confusion are medicines with anticholinergic properties. A number of Australian studies have examined the extent to which people living in aged care take medicines with anticholinergic properties, with collective results suggesting 40% to 50% of people living in aged care are taking medicines with anticholinergic properties. The largest study, involving over 17,000 people living in aged care in 2013, found that across a one year time frame, 46% of all people use medicines with moderate to strong anticholinergic properties at some point in time during the year; this rose to 52% when limited to people with dementia.[47] This is a finding that raises concern because use of medicines with anticholinergic properties can worsen cognitive function.

A smaller study in Western Australian involving 351 people with dementia living in aged care[34] found that four in five people were taking at least one medicine with anticholinergic properties. Another Australian study involving 602 people living in aged care found 34% were taking at least one anticholinergic medicine, while 18% were taking a medicine that had anticholinergic properties together with a medicine that had sedative properties.[48] The frequent use of medicines with anticholinergic properties is further confirmed by a study which reviewed 814 reports by pharmacists undertaking medicines reviews in the aged care setting.[49] It used different methods for assessing anticholinergic medicine use and found between 36% and 67% of people living in aged care were prescribed at least one anticholinergic medicine.[49]

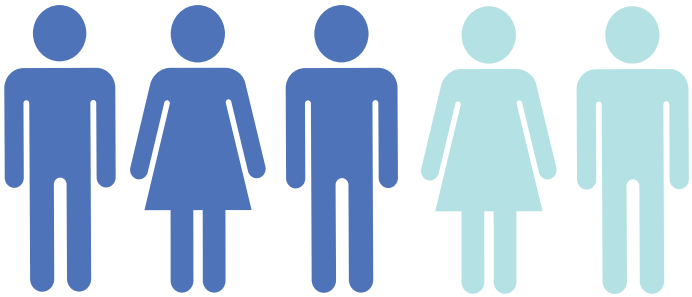
Using two medicines that have anticholinergic properties at the same time, more than doubles an older person's risk of being admitted to hospital for confusion, delirium or dementia.

Figure 5: Number of anticholinergic medicines used concurrently and risk of hospital admission for confusion or dementia



An Australian study has demonstrated the harm that can be associated with anticholinergic use, particularly where two or more medicines with anticholinergic properties are used together.[44] Older people on two anticholinergic medicines together have 2.5 times the risk of being admitted to hospital for confusion, delirium or dementia, than older people not taking these medicines (**Figure 5**).

Medicines with sedative properties



Up to 60% of people living in aged care are taking medicines with sedative properties; with one quarter taking two or more concurrently.

The group of medicines known as psychotropic medicines include many of the medicines used to treat mental health conditions, including antipsychotics, antidepressants and medicines for anxiety. Many of these medicines have sedative effects, which can result in drowsiness or over-sedation if too much is used. Psychotropic medicines are commonly prescribed for people living in aged care facilities in Australia. A national study among 11,368 people from 139 aged care facilities found that almost two-thirds (61%) were taking psychotropic medicines regularly and a quarter of people living in aged care were taking two or more psychotropic medicines concurrently.[50]

The 2019 Royal Commission into Aged Care Quality and Safety Interim Report highlighted the potential for over-use of psychotropic medicines.[25] An expert panel was asked to assess the appropriateness of use of psychotropic medicines in people living in aged care. The panel estimated that in only 10% of cases where psychotropic medicines were prescribed were justified.[25]

Australian studies have demonstrated the potential for harms in older persons from using medicines with sedative properties, particularly where two or more medicines with sedative properties are used together. Older people on two medicines with sedative properties have double the risk compared to people not taking these medicines of being admitted to hospital for falls or confusion (**Figures 6** and **7**).[45,51]

Figure 6: Number of medicines with sedative properties used concurrently and risk of hospital admission for falls.

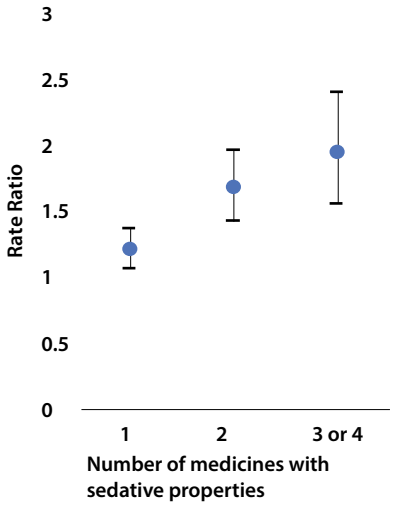
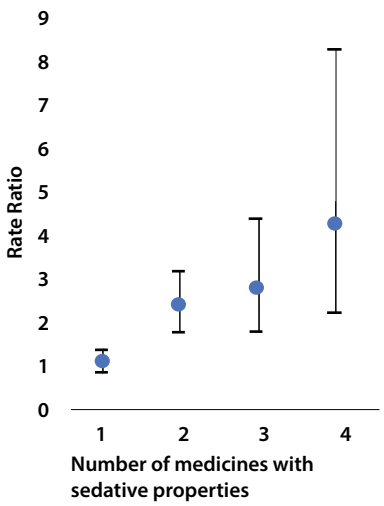
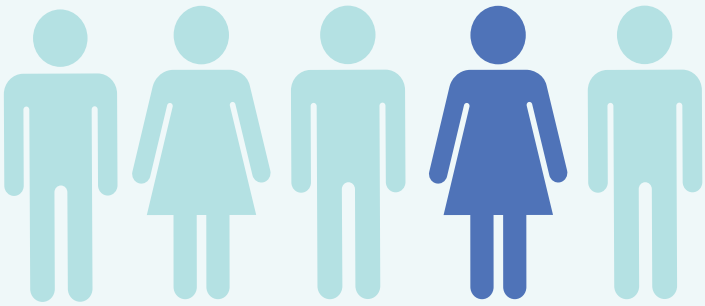


Figure 7: Number of medicines with sedative properties used concurrently and risk of hospital admission for confusion, delirium or dementia.



USING MEDICINES FOR TOO LONG



One-fifth of people living in aged care are taking antipsychotics; more than half use the medicine for too long.

Studies have demonstrated that antipsychotic use in older people is associated with increased risk of hospitalisation for hip fracture and pneumonia, as well as increased risk of stroke and death.

Antipsychotics

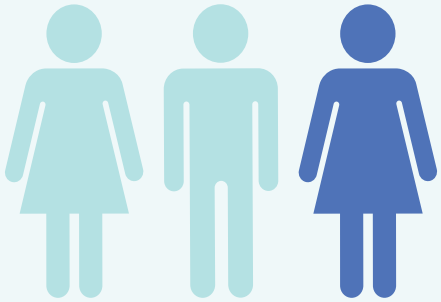
As described earlier, some medicines are considered appropriate for short term use, but inappropriate when used long term. Antipsychotics and benzodiazepines are both classes of medicines where there may be some benefit in some people for short term use, but long term use is not recommended in most people.

Antipsychotic use is frequent among people living in aged care in Australia. A 2019 study that included 97,739 people living in aged care facilities found that over 20% of people were using an antipsychotic at the time they entered the aged care facilities.[52] Other Australian studies assessing use of antipsychotics in people living in aged care (after admission) have found similar estimates. One, involving 11,368 people living in 139 aged care facilities across Australia in 2014/15 found that that 22% were using antipsychotics on a regular basis.[50] Another, involving 4,775 people living in 71 aged care facilities in New South Wales and the Australian Capital Territory in 2015 found that one in five were using an antipsychotic.[53] While a third study, based on health claims data from 14,237 people living in aged care in 2015/16 found one fifth were dispensed antipsychotics.[54]

The duration of antipsychotic use among people living in aged care has also been found to be longer than recommended. A study among 5,825 people with dementia living in 68 aged care facilities in New South Wales and the Australian Capital Territory between 2014 and 2017 found two-thirds were on antipsychotics for longer than three months.[55] A New South Wales study involving 291 people with dementia living in 40 aged care facilities between 2009 and 2011 found that half of all people with dementia used antipsychotics medicines for more than six months.[56] A third study, based on health claims from 14,237 people living in aged care facilities found half of all people using antipsychotics used them for six months or longer.[54] This same study examine one specific antipsychotic, which was risperidone. Risperidone may be used for behavioural and psychological symptoms of dementia after non-medicine therapies have failed. The study found half of all people using risperidone used it for at least eight months. At the time of this result, the recommended duration of risperidone was that use for behavioural and psychological symptoms of dementia should not exceed 12 weeks (three months).[57]

The frequent use of antipsychotics in older people living in aged care is likely to be associated with harm. Australian and international studies have demonstrated that antipsychotic use in older people is associated with increased risk of hospitalisation for hip fracture and pneumonia, as well as increased risk of stroke and death.[58,59]

Up to one-third of people living in aged care are taking benzodiazepines; more than half use the medicine for too long.



Benzodiazepines

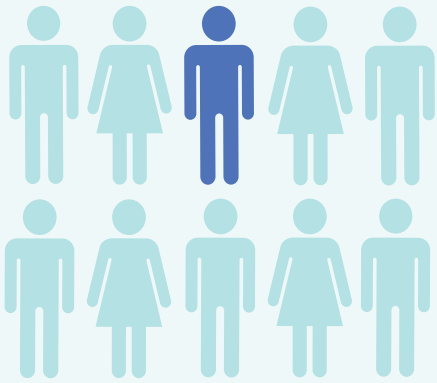
Benzodiazepines are another psychotropic medicine that are not recommended long term in older people as their use is associated with side effects including increased risk of developing delirium and falls.[51,60] Despite this, Australian studies have found that use of benzodiazepine medicines in older people is frequent; with between one fifth and one third of people living in aged care receiving benzodiazepines. A 2014/15 national study involving 11,368 people living in 139 facilities found that more than one in five people were using benzodiazepines on a regular basis.[50] Another study involving 14,237 people living in aged care facilities in 2015/16 found that more than one-third were dispensed benzodiazepine in the one year period.[54]

Similarly to the findings with regards to antipsychotics, there is evidence that the duration of benzodiazepine use in aged care is too long, with one study involving over 14,000 people finding that 50% of people using a benzodiazepine used it for eight months or more.[54]

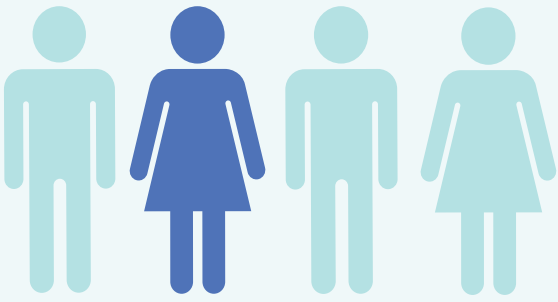
Non-steroidal anti-inflammatory medicines

Medicines known as non-steroidal anti-inflammatory agents are only indicated for short-term use to treat pain and inflammation. These medicines are not recommended long term and are considered potentially inappropriate for many older people.

Australian studies suggest up to one in ten persons living in aged care are prescribed a non-steroidal anti-inflammatory. A study involving 10,367 people from 68 residential aged care facilities across New South Wales and the Australian Capital Territory between 2014 and 2017 found one in ten people used an oral non-steroidal anti-inflammatory medicines.[21] Similar estimates were obtained from a 2015/16 study that used health claims data from over 14,000 older persons living in aged care.[54] The study found that one in ten people were dispensed a non-steroidal anti-inflammatory medicine; of these, more than a quarter used the medicines long-term.[54]



One in ten people living in aged care are prescribed a non-steroidal anti-inflammatory medicine.



At least a quarter of people living in aged care on non-steroidal anti-inflammatory medicines use the medicine for too long.

Proton pump inhibitors

Half to three-quarters of people on proton pump inhibitors use the medicine for too long.

Proton pump inhibitors are medicines used to treat gastric ulcer and gastroesophageal reflux disease (heart burn). The recommended period of use is for eight weeks. Inappropriate long term use of proton pump inhibitors has been observed in half to three-quarters of people living in aged care who use these medicines. A study involving 383 people living in six South Australian aged care facilities found that among the 123 people who had gastroesophageal reflux disease or dyspepsia, three-quarters used the medicine for longer than recommended.[61] A larger study, based on health claims data from over 14,000 persons living in aged care, found that among people who used proton pump inhibitors 50% used them for at least 360 days in a year.[54]

Use of proton pump inhibitors is associated with increased risk of harm, with a 2019 review which combined data from multiple studies showing that long-term proton pump inhibitor users have increased risk of hip fracture.[62]

Antimicrobials

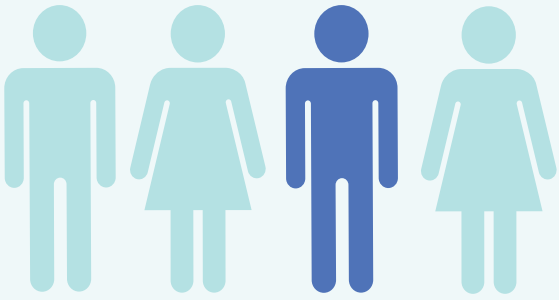
Antimicrobials are medicines used to treat infections caused by bacteria, virus and fungi. Short term use of antimicrobials are recommended for most infections. Inappropriate use of antimicrobials can contribute to antimicrobial resistance, where the medicines used are no longer effective at treating infections.

One national study suggests inappropriate antimicrobial use in aged care facilities in Australia.[63] The 2018 Aged Care National Antimicrobial Prescribing Survey involving 20,030 people from 407 aged care facilities across Australia found that one in ten people used at least one antimicrobial on the day of the survey.[63] About two-thirds of antimicrobial medicines prescribed were for people without documented signs or symptoms of a suspected infection in the week prior to starting the medicine. The most commonly prescribed antimicrobials were cefalexin, an anti-bacterial used to treat infections such as respiratory tract infections and urinary tract infections, and topical clotrimazole, an anti-fungal medicine used to treat skin infections. About half of people prescribed cefalexin or topical clotrimazole used the medicines for longer than six months.

INAPPROPRIATE PRESCRIBING OF RENALLY CLEARED MEDICINE

As people age, kidney function is often reduced. This has the potential to affect medicine use because the kidneys are the primary mechanism for eliminating many medicines from the body. If the kidneys cannot efficiently eliminate the medicines, the medicines will accumulate in the body and this increases the risk of toxicity. Almost a third of people aged 75 years and over have abnormal kidney function,[64] which means prescribing of medicines cleared by the kidney can be particularly problematic in older people.

Two Australian studies have reported the prevalence of inappropriate prescribing of renally cleared medicines in people with poor renal function living in aged care. A study involving 172 people with chronic kidney disease in 2011/12 found 16% were prescribed an inappropriate dose of a renally cleared medicine for their level of renal function.[7] Another study in 720 people living in aged care facilities with poor renal function found inappropriate prescribing of at least one renally cleared medicines in 38% of people.[65]



About one in four people with poor kidney function are prescribed an inappropriate dose for medicines cleared by the kidney.

MEDICINE REGIMEN COMPLEXITY

The more medicines a person is taking, the more complex the medicine regimen is likely to become. Factors that make medicine regimen complicated include how many different formulations of the medicines that a person takes (e.g. tablets, sprays, drops, nebulisers), how many times across the day that a medicine needs to be taken (e.g. once daily, every two hours, when necessary) and how complex the directions are to follow (e.g. dissolve tablet, take with food).[66] More complex medicine regimens are associated with reduced adherence to medicines in people living in the community.[67] In the aged care setting, where medicines are administered by care staff, the complexity of a medicine regimen may not affect adherence to medicines, but does require more staff time for administration activities.

A measure commonly used in the academic literature to determine medicine complexity is the 65-item Medication Regimen Complexity Index.[66] The Medication Regimen Complexity Index scores are added up for each medicine that a person is taking, and so there is no maximum score. A higher score means a more complex medicine regimen.

Three Australian studies examined the complexity of medicines taken by people living in aged care facilities.[68-70] All studies used the Medication Regimen Complexity Index to measure medicine complexity. The Medication Regimen Complexity Index scores ranged from 26 to 44. However, it is difficult to interpret what the score means for an individual because there is no maximum or cut off score for the Medication Regimen Complexity Index.

An Australian study developed and validated the Medication Regimen Simplification Guide for Residential Aged CarE (MRS GRACE), a tool to simplify the medicine regime for people living in aged care facilities.[71] Using the tool, two pharmacists were able to simplify medicine regimen in up to 60% of people.[71] The tool is currently being tested in a larger trial[72] to evaluate uptake of the recommendations and its long-term impact on outcomes including falls and hospitalisations.

UNDERUSE OF MEDICINES

While the previous sections focused on potential harm resulting from using medicines, underuse of medicines is also a problem that has been identified for people living in aged care. Underuse of medicines can make people more vulnerable to avoidable diseases and their complications. Underuse of medicines in aged care has been less well studied than over-use of medicines, however an Australian study provide some insight into under-use of medicines for heart disease.

An Australian study evaluating medicine use in 17,672 people living in aged care in 2013 found underuse of recommended cardiovascular medicines.[47] Among people with a history of ischaemic heart disease or post heart attack, only 48% received recommended medicines for high cholesterol and 54% received a beta-blocker. Statins and beta-blockers are used to prevent recurrence of ischaemic heart disease and heart attack.

Box 4: Case study

Opioid overdose resulting in death

A person was prescribed morphine **2.5–5 mg subcutaneous injection**. The direction on the medicine chart was 2.5–5 mg morphine every four hours. The nurse incorrectly read the ampoule packaging as 1 mg/1 ml instead of 10 mg/1 ml, and so drew up 2.5 ml. Prior to administration, the medicine was double checked by an extended care assistant but the error was not picked up. This resulted in the person taking a dose of **25 mg**. The person died as a result of opioid overdose.

Comment: The tragedy could have been prevented if more stringent safeguards were in place. Administration of high-risk medicine such as morphine should be verified by a second person who is a qualified nurse.

Source: *Magistrates Court of Tasmania Coronial Division 2013*[73,74]

ADMINISTRATION ERRORS

Medicine-related problems can occur at many different points during the process of using medicines including during prescribing, dispensing and administration. In this section, we focus on problems that occur during administration of the medicines.

DOSE ADMINISTRATION AID ERRORS

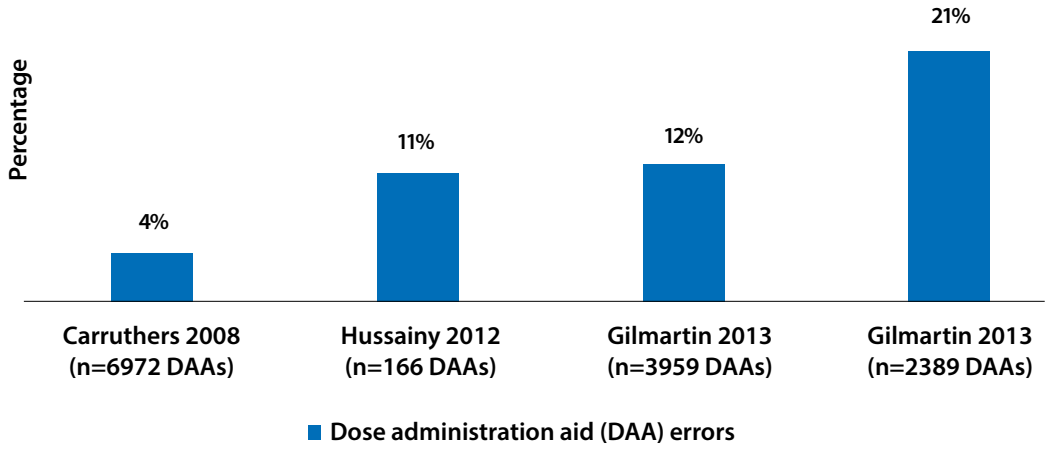
Dose administration aids are used in residential aged care facilities to support medicine administration. Dose administration aids enable medicines to be packaged into separate units according to the times of day the medicines are to be taken. There have been four Australian studies assessing the frequency of medicine packing errors in dose administration aids (**Figure 8, Appendix 3**).[75-78]

The studies reported a rate of packing error between 4% and 21% per number of dose administration aids. The weighted average error rate is 9% when taking into account the different number of dose administration aids assessed in each study.[75-78] Common types of errors included incorrect dose packed, supply of a ceased medicine, packaged at the incorrect time and omitted medicines.

Errors have been found to occur in, on average, 9% of dose administration aids.

Factors contributing to errors included failure to document or communicate changes in the medicine regimen, lack of supply of prescription, and illegible prescription or chart, with one study showing a quarter of errors occurred for these reasons.[75] This same study showed the error was considered to have originated in the pharmacy in 40% of occasions.[75]

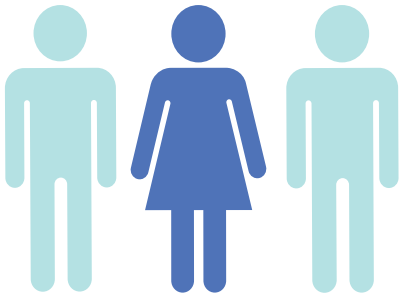
Figure 8: Percentage of dose administration aid errors in residential aged care facilities.



INAPPROPRIATE ALTERING OF MEDICINES

Some people who have difficulty swallowing medicines may have their medicines crushed or altered before taking them. However, not all medicines are able to be altered and there are potential problems with this practice.[79] Altering medicines may lead to increased toxicity, reduced effectiveness, altered absorption and stability or create potential safety hazards because the medicines no longer works in the way they were originally intended.[79]

Australian evidence suggests medicines are frequently altered when administered to older people living in aged care facilities.



Up to one-third of people living in aged care facilities have their medicines altered.

15% to 32% of the medicines that were altered should not have been altered.

Box 5: Case study

Inappropriate crushing

Due to difficulty swallowing medicines in a woman living in an aged care facility, a speech pathologist recommended that all medicines should be crushed prior to administration. A pharmacist reviewed all medicines to check suitability for crushing. One medicine was identified that should not be crushed because it was formulated as a slow release preparation, potassium chloride. The pharmacist recommended using a soluble form of potassium chloride instead.

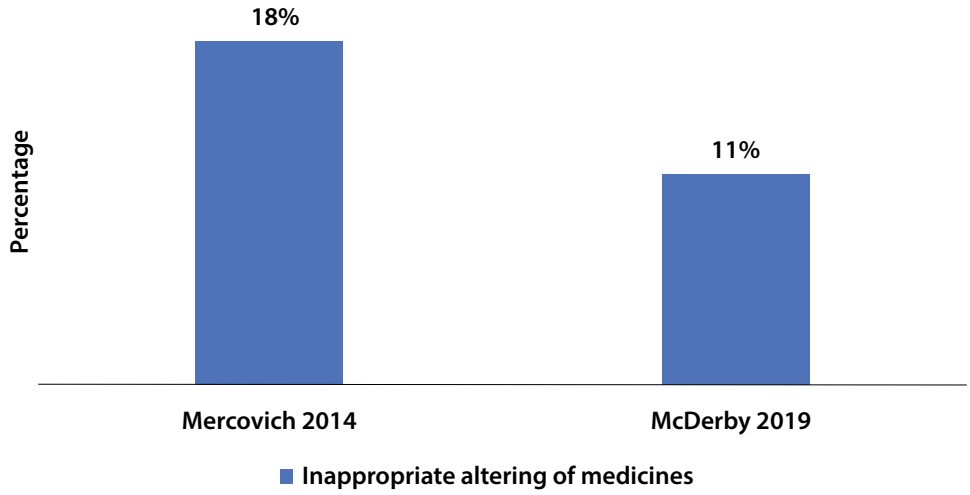
Comment: Crushing potassium chloride results in the release of the medicine all at once, which may increase the risk of side effects such as vomiting and abdominal discomfort.

Source: *McDerby et al 2019*[80]

In 2002, a South Australian study in 10 aged care facilities reported that one-third of the 1,207 observations of medicine administration involved at least one medicine being administered in an altered form.[81] Of the medicines that were altered, 17% had the potential to cause increased toxicity, decreased efficacy, unpalatability, safety or stability concerns.[81] Further, there was spillage or loss of medicine in 70% of the cases,[81] for example when the powder was trapped in the crushing devices or left in the mortar and pestle. The consequence of spillage or loss is that the person receiving the medicine may not be given the full dose.

Two more recent studies investigated the same issue (**Figure 9**). In 2014, a study involving 160 people living in two aged care facilities in the Australian Capital Territory reported that almost one in five (18%) people had their medicines altered prior to administration.[82] A total of 75 medicines were altered; of these, 32% were not appropriate for altering.[82] In 2018, another study conducted in the Australian Capital Territory reported that 11% of people living in aged care had their medicines modified prior to administration.[83] A total of 221 medicines were altered; of these, 15% were inappropriate for altering.[83]

Figure 9: Percentage of people living in aged care facilities who had their medicines inappropriately altered.



DEVIATIONS DURING MEDICINE ADMINISTRATION

Nursing staff often follow a standard work process when administering medicines to people living in aged care facilities.[84] When this workflow is not adhered to, there is a risk that the deviation from the work process may lead to patient harm. A number of factors determine whether or not the deviation would result in harm. These factors include whether the deviation is picked up at all, and if detected, whether it is before or after medicine administration, whether the medicine has a high risk of causing injury or death, and the person's condition because frail older people are more vulnerable to harms.

We highlight a small study which looked at deviations during medicine administration.[84] The study examined medicine administration process by nursing staff in a 78-bed aged care facility in Australia in 2013.[84] In twelve medicine rounds performed by seven staff (one registered nurse, four enrolled nurses and two personal care workers), a total of fifteen process deviations were observed. Examples of process deviations included:

- Nurses documenting administration of the medicine in the medicine record before administering a medicine.
  Comment: This could lead to missed medicine administration if an interruption occurred and the nurse could not remember if the medicine was administered or not.
- Enrolled nurses and personal care workers administering "when required" medicine to people without seeking permission of the registered nurse on duty.
  Comment: "When required" medicines are usually written with a direction for use e.g. for pain, for agitation. Inappropriate use occurs when the symptom is not present or not serious enough for medicine use, or if the medicine is administered too frequently. Inappropriate use of "when required" medicines that have sedative effects can have consequences if too much medicine is used; which include excessive sedation leading to decline in physical and cognitive function, falls or hospitalisations.
- Nurses prepared medicines for two people at the same time.
  Comment: Medicines may be administered to the wrong person if the nurse wrongly identifies the person who should be taking the medicine.
- Nurses did not measure the liquid medicine at eye level.
  Comment: This could lead to incorrect dosing.
- Nurses waited only for a few seconds between multiple inhalations.
  Comment: Inhaler medicines for symptom relief are more effective if there is an interval between inhalations.

PROBLEMS DURING TRANSITION TO AGED CARE

People are particularly vulnerable to medicine problems when they transition between the health system and residential aged care facilities. For example, the types of medicine or the dose of medicines that a person is on may change following admission to hospital. If the changes are poorly communicated to the staff at the residential aged care facility when the person is discharged from hospital there is potential for medicine-related problems to occur. Previous Australian studies have shown that missed or delayed administration of doses of medicines were common when a person was discharged from hospital back to a residential aged care facility.[85,86] These studies were undertaken prior to the implementation of the national residential medicine chart.[87] No more recent studies were located that reported the frequency of medicine-related problems for older persons discharged from hospital to residential aged care.

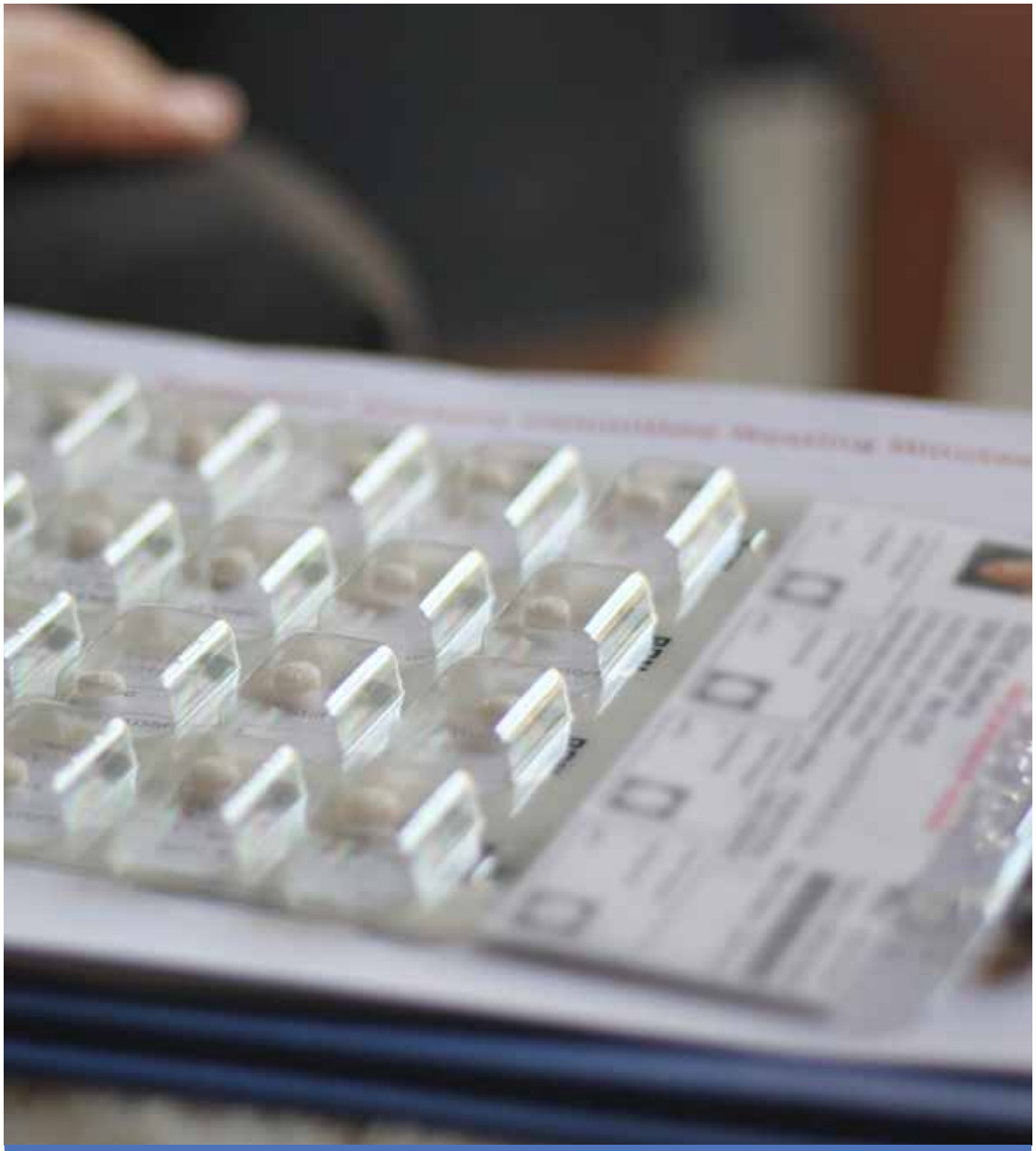
Admission to aged care is another transition of care where medicine errors can occur. No Australian studies have assessed medicine errors at admission to aged care; however, studies have examined changes to medicine use upon admission to aged care.[52,88] An Australian study using the Registry of Senior Australians examined the prevalence of antipsychotic use prior to and after entering residential aged care facilities in Australia.[52] The study which included 97,739 people living in aged care facilities showed an increase in antipsychotic use. Approximately 6% of people were using antipsychotics nine months prior to entering the facilities. This rose to over 20% of people using antipsychotics upon admission into the aged care facilities.

Box 6: Case study

Missed dose increases risk of a thromboembolic event

A pharmacist reviewed the medicines of a woman who transferred from the hospital to the aged care facility. The pharmacist identified several medicine-related problems including missed medicines, incorrect number of capsules supplied and medicines written on the wrong chart. The pharmacist identified that the person had not received any warfarin, a medicine to prevent blood clots, since entering the facility eight days earlier because warfarin had been prescribed as "when required". This resulted in under-dosing which could be seen by the blood test to measure the level of coagulation. A sub-therapeutic coagulation level was detected (International Normalised Ratio (INR) = 1.1). This has the potential to be harmful to the person as the medicine is to prevent blood clots and too low a dose would not be effective in preventing blood clots. The woman was re-started on warfarin and achieved therapeutic INR.

Source: *McDerby et al 2019*[80]



Box 7: Case study

Overdose that can potentially lead to death

An 86-year-old man with diabetes, osteoarthritis and high blood pressure was admitted to hospital for community acquired pneumonia. Prior to hospital admission from the aged care facility, he was taking glipizide 10 mg and metformin 1000 mg daily for his diabetes. Due to fluctuating blood glucose levels while he was in the hospital, the diabetic medicines were temporarily stopped and insulin 20 units at night was initiated. Upon discharge, the doctor who completed t he discharge medicine chart mistakenly included the man's usual medicines and the insulin. The nurse at the aged care facilities did not identify that the order for both oral medicines and insulin was an error. The nurse administered the medicines as ordered. The man was found to be cold and unresponsive with a blood glucose level of 2.1 mmol/l, and was immediately sent to the hospital. The man made a full recovery.

Source: *Gilbert et al 2018*[89]

OPPORTUNITIES FOR IMPROVEMENTS

There are significant opportunities for improving medicine use and reducing medicine-related harm in aged care.

Supporting improvements on transition into residential aged care

A person's transition into aged care provides a time to optimise medicine use. Current research suggests this is a time where many medicines, including antipsychotics, antidepressants and benzodiazepines, are started and then continued.[52,88] These medicines have the potential to cause sedation and confusion and increase risk of adverse outcomes including falls and delirium.

Mechanisms to optimise medicine use at the point of transition are required, such as medication action plans, which include the rationale for any new therapies started, the timeline for ceasing the medicine, and active methods for monitoring the potential harms from the medicine; most notably sedation and confusion.

Supporting improvements in medicine administration

Medicine regimens in persons living in aged care are usually complex and, while research is limited to one Australian study, it suggests the regimen can be simplified in up to 60% of cases.[70] Simplification of the medicine regimen has many potential advantages, including potential for reduced errors, reduced staff time spent on medicine administration and reduced pharmacist time spent on medicine packing. Tools such as the Medication Regimen Simplification Guide for Residential Aged CarE (MRS GRACE)[71] are being trialled and it will be important to examine the impact of these types of tools on error rates and staff time in the aged care setting to inform widespread implementation.

Three Australian studies have shown that alteration of medicines in the aged care setting to support medicine administration is frequent, and that in up to one third of cases alteration of the medicine has the potential to cause problems. Mechanisms to enable regular consultation and documentation between aged care staff and pharmacists are required to ensure pharmacists are aware of people with specific requirements for medicine administration (e.g. difficulty swallowing, poor dexterity) and where alternative formulations may be required. Protocols are necessary to ensure staff in the aged care facility are aware of the need to consult pharmacists prior to establishing processes to alter medicines. Facilities could consider pharmacist review of administration practices to support quality improvement activities.

Supporting improvements in medicine dosing

As many as 50% of all people living in aged care have reduced renal function.[7,90,91] Prevention of inappropriate dosing or selection of medicines for people with renal impairment would be possible if pharmacists have information on an individual's renal function. Mechanisms to provide pharmacists with information on an individual's renal function are necessary to ensure dosing errors and medicine selection errors are detected at the time a medicine is first prescribed or dispensed. My Health Record provides one option for this if relevant pathology records have been uploaded in the record; however, mechanisms for direct reporting of renal function to pharmacists are also required.

Reducing medicine-related problems

Medicine-related problems can occur when a person's characteristics are not fully considered (for example renal function is not taken into account or a concurrent illness is not considered), however, they can also occur at the organisational level due to facility factors. Australian research has shown that the key determinant of use of medicines prescribed as "when required" was the aged care facility, with the individual person's characteristics having less influence.[92]

While collectively, Australian research shows that at least half of all people living in aged care are prescribed at least one medicine with sedative or anticholinergic properties, there is also considerable variability in the use of these medicines between facilities. This suggests that in addition to individual factors, facility factors may be contributing to use. Mechanisms employed in other settings to identify systems related problems contributing to medicine problems include facility wide medicine use evaluation within quality improvement cycles.

Facility wide audit and feedback with review by a Medication Advisory Committee is a potential mechanism to identify over-use of medicines at the facility level and potential systems contributors and solutions. Audit and feedback examining the extent of administration of medicines prescribed for use "as required" will also be necessary. The potential for harms from administration practices related to medicines to be used "as required" needs to be examined within the context of each person's medicine regimen, including cumulative use of medicines with sedative or anticholinergic properties. Regular multidisciplinary review of the facility wide extent of administration of medicines to be used "as required", including reason for use and cumulative dose may identify systemic problems related to over-use and potential chemical restraint, as well as support quality improvement activities.

The residential medication management review program is in place for identifying medicine-related problems at an individual level.[93] Australian evidence consistently shows that at the time medicine reviews are implemented, medicine-related problems are identified in nearly all people who receive a review and that the service is effective in resolving many medicine problems.[5-7] However the service is implemented infrequently and identifies problems after they occur. Mechanisms for supporting ongoing medicine review and continual revision of medication action plans to optimise medicine use are likely to be beneficial. These mechanisms need to include provision of information to the whole health care team, including pharmacists with responsibility for dispensing medicines to the facilities. In particular, knowledge of the adverse medicine events detected during medicine reviews need to be provided to the whole health care team to support ongoing adverse event prevention.

Supporting improvements in monitoring for signs of toxicity

A review of coronial investigations into medicine-related deaths found that failure to review people for signs of toxicity or to recognise signs of toxicity was a factor in four of the deaths (**Box 8**).[94] Failure to recognise the side effects of sedation or confusion due to medicine use can also lead to the adverse outcomes of falls or delirium. Falls are a frequent occurrence in the aged care setting, with one hospital admission for a falls-related injury for every five people living in aged care each year.[95]

The frequency of delirium events in people living in aged care in Australia has not been reported; however, international estimates suggest at least 10% of people living in aged care experience delirium.[96,97] Medicines are implicated in both falls and delirium. Falls and delirium events should both be a trigger for a medicine review. Consideration could be given to proactively monitoring changes in a person's cognition and mobility, including gait and balance, using validated tools[98] when medicines with sedative or anticholinergic properties are added to the medicine regimen. Cessation of medicines may need to be considered when cognition or mobility is affected. In addition, facility-wide audit and feedback on rates of these events may support quality improvement opportunities, as variation in the rates of these events facility to facility have been reported.[99]

Box 8: Case study

Coronial investigations into medicine-related deaths in aged care facilities

There have been 30 coronial investigations into medicine-related deaths occurring in aged care facilities between July 2000 and July 2013.
Thirteen cases described the nature of the medicine errors which resulted in death.
Nine deaths occurred due to an administration error and four due to monitoring errors:

Administration

- In four cases the medicine was given to the wrong person
- In three cases self-medication with an opioid or antidepressant contributed to the death
- In one case the wrong dose of medicine was given
- In one case the infusion pump rate was wrong

Monitoring

- In four cases there was potential failure in reviewing or recognise signs of toxicity

Recommendations from the coronial investigations were to:

- increase education and training of aged care staff on dose administration aids;
- have collaborative review between relevant regulatory bodies to determine the need for regulation of personal care workers; and
- implement protocols to monitor renal function for people on digoxin.

Source: *Jokanovic et al 2019*[94]

PSA CONCLUSION AND RECOMMENDATIONS

It is clear that more needs to be done for residents in aged care facilities across Australia to reduce the harm associated with medicines. The PSA believes the following actions directed at reducing medicine harm, some of which were recommended in the Royal Commission into Aged Care Quality and Safety's Interim Report, should be implemented as a matter of priority:

1 Physically embed pharmacists within aged care facility teams by increasing funding allocations to Residential Medication Management Reviews (RMMR) and Quality Use of Medicine (QUM) Services, sufficient to provide at least 0.6FTE per 100 aged care residents.

2 Provide the opportunity for pharmacists to engage in a cycle of care through the delivery of follow-up medication reviews to patients at risk, and remove the caps on the number of medicines reviews that pharmacists can perform to ensure that those elderly patients at risk of medicine-harm receive appropriate care.

3 As a matter of priority, the Commonwealth Government should adopt the recommendations of the MBS review taskforce by ensuring that pharmacists are remunerated to participate in case-conferencing for residents within aged care facilities.

4 Provide targeted activities delivered by pharmacists, such as the RedUSe program, funded under the QUM program. This would allow pharmacists to undertake audits of prescribing and provide feedback, and enable education to aged care facility staff and GPs in core medicine areas such as psychotropic medication use, opioids, deprescribing and antimicrobials.

5 Provide funding to aged care facilities to implement contemporary electronic medication management solutions, including prescribing, dispensing and administration.

6 Establish a Medicine Safety in Aged Care Resource and Support Program by allocating $8.7M over four years to support clinical governance of medicines management within aged care.

7 Allocate $2M for the implementation of Clinical Governance Principles for Pharmacy Services within Residential Aged Care Facilities. This robust framework can be used by pharmacists to guide service delivery that is safe, of high quality and clinically appropriate.

8 Similar to patients in the community, residents of aged care facilities should have equitable access to subsidised DAA services where clinically warranted and where the use of a DAA is mandated by the facility.

9 Allocate $15M through a targeted call for proposals through the Medical Research Future Fund (MRFF) to develop and trial interventions designed to reduce harm associated from medicines for older Australians.

10 Develop a standard comprehensive set of safety and quality use of medicine indicators for aged care facilities, and require facilities to regularly report outcomes against these measures.

RedUSe

Reducing **U**se of **Se**datives

Audit

Education

Review


Yanni

TECHNICAL APPENDIX

APPENDIX 1:
SEARCH STRATEGY

Australian literature on medicine safety (from 2014 to October 2019) were identified from the following databases: Medline, Pubmed, Embase and Ovid Emcare. Criteria for inclusion of studies are that the studies address medicine-related problems including adverse medicine events, adverse medicine reactions or medicine incidents as a result of the therapeutic prescribing, dispensing or administration of medicines. The literature was restricted to studies in Australian residential aged care facilities. Reference lists of relevant studies were reviewed to identify additional papers. Australian case studies on medicine-related problems were identified and included in this report where relevant.

Studies included in the 2019 Medicine Safety: Take Care[100] and the 2013 Australian Commission on Safety and Quality in Health Care Medication Safety[101] reports were extracted and collated in the current report. The Royal Commission into Aged Care Quality and Safety Interim Report,[25] national or state reviews and annual reports of the aged care sector were reviewed to identify additional data on medicine-related problems.

Literature search results

The literature search of the electronic databases identified 516 (Medline), 582 (PubMed), 1400 (Embase) and 369 (Ovid Emcare).

Example search strategy

Database: Ovid MEDLINE(R) ALL <1946 to October 31, 2019>

1 Medication Reconciliation/ or Medication Errors/ (13546)
2 Diagnostic Errors/ or Medical Errors/ (52746)
3 Safety Management/ (19642)
4 "Quality of Health Care"/ (70612)
5 "Drug-Related Side Effects and Adverse Reactions"/ (30696)
6 Quality Assurance, Health Care/ (55254)
7 Patient Safety/ (17966)
8 patient* safety.mp. (41313)
9 medication* safety.mp. (2111)
10 adverse drug event*.mp. (3715)
11 adverse drug react*.mp. (20038)
12 medica* incident*.mp. (311)
13 medica* mishap*.mp. (54)
14 medica* mistake*.mp. (213)
15 medica* misadventure*.mp. (118)
16 drug misadventure*.mp. (15)
17 drug* toxicity.mp. (5437)
18 medication related harm*.mp. (50)
19 medication related incident*.mp. (22)
20 medication related problem*.mp. (455)
21 medication reporting system*.mp. (1)
22 pharmaceutical reporting system*.mp. (0)
23 medic* prescri* error*.mp. (68)
24 drug* prescri* error*.mp. (19)
25 prescri* error*.mp. (1053)
26 medica* dispensing error*.mp. (24)
27 drug* dispensing error*.mp. (16)
28 dispensing error*.mp. (276)
29 medication* administra* error*.mp. (327)
30 drug* administra* error*.mp. (110)
31 administra* error*.mp. (888)
32 medication* related admission*.mp. (9)
33 drug related admission*.mp. (51)
34 Patient Transfer/ (7966)
35 medic* review*.mp. (2889)
36 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 (289072)
37 Australia/ or Australian Capital Territory/ or New South Wales/ or Northern Territory/ or Queensland/ or South Australia/ or Tasmania/ or Victoria/ or Western Australia/ or Australia.mp. or Victoria.mp. or Tasmania.mp. or New South Wales.mp. or Queensland.mp. or Australian Capital Territory.mp. or Australia*.mp. (197040)
38 Homes for the Aged/ or "Aged, 80 and over"/ or Aged/ or Nursing Homes/ or residential facilities/ (3016975)
39 (aged care or nursing home* or residential adj3 facilit* or care home*).mp. (46671)
40 exp Home Nursing/ (9274)
41 38 or 39 or 40 (3028276)
42 36 and 37 and 41 (1380)
43 limit 42 to yr="2014 -Current" (516)

APPENDIX 2:
PREVALENCE AND TYPES OF MEDICINE-RELATED PROBLEMS

	STAFFORD 2009[4]	NISHTALA 2011*[5]	KAUR 2012[6]	GHEEWALA 2014[7]
Number of residents (number of aged care facilities)	96	500 (62 facilities)	296 (6 facilities)	847
State	Various	NSW	Queensland, NSW	NSW
Percentage (%) of people with medicine-related problem	100	96	-	98
Total number of medicine-related problems	375	1433	802	2712
Average problem per person	3.9	3	2.7	3.2
Types of medicine-related problems				
Untreated indication, n (%)	**53 (14.1)**	-	**198 (24.6)**	**608 (22.4)**
Medicine selection problems, n (%)	**99 (26.3)**	-	**72 (8.9)**	**512 (18.9)**
Duplicate, n (%)	*1 (0.3)*	-	*38 (4.7)*	*5 (0.2)*
Medicine-medicine interaction, n (%)	*53 (14.1)*	-	*24 (2.9)*	*99 (3.6)*
Wrong dosage form, n (%)	*3 (0.8)*	-	-	-
Adverse medicine reactions, n (%)	**79 (21)**	-	**118 (14.7)**	**419 (15.4)**
Monitoring issues, n (%)	**49 (13)**	-	**160 (19.9)**	**217 (8)**
Inappropriate dose, n (%)	**45 (12)**	-	**127 (15.8)**	**221 (8.1)**
Over-dose, n (%)	*16 (4.3)*	-	-	*81 (2.9)*
Under-dose, n (%)	*4 (1.1)*	-	-	*53 (1.9)*
Compliance, n (%)	**5 (1.3)**	-	-	**119 (4.4)**
Education, n (%)	**13 (3.5)**	-	-	**3 (0.1)**
Not classifiable, n (%)	**33 (8.8)**	-	-	**613 (22.6)**

*The study categorised findings for medicine-related problems into three main groups - indication, effectiveness and safety. Results according to different types of medicine-related problem were not reported.

APPENDIX 3:
MEDICINE-RELATED PROBLEMS IN DOSE ADMINISTRATION AIDS

REFERENCE	Sample size	Prevalence of medicine-related problems	Average number of medicine-related problems	Risk of harm associated with medicine-related problems
Carruthers 2008[75]	6972 DAAs	4.3% (297 DAAs with packing incident)	Not reported	Not reported
Hussainy 2012[76]	166 DAAs	10.8% (18 DAAs with packing incident)	Not reported	67% (12) incidents deemed to be significant or have potential to cause harm
Gilmartin 2015[77] All DAAs (blister pack or sachet)	3959 DAAs	11.5% (457 DAAs with ≥1 packing incident)	1.5 per DAA (684 incidents, in 457 DAAs)	*DAAs with incidents rated as: Insignificant risk: 76 Minor risk: 184 Moderate risk: 107 Major risk: 136 Catastrophic risk: 2
Gilmartin 2015[77] Blister pack DAAs only	2920 blister pack DAAs	10.5% (306 blister pack DAAs with ≥1 packing incident)	1.4 per blister pack (434 incidents, in 306 blister packs)	
Gilmartin 2015[77] Sachet DAAs only	1039 sachet DAAs	14.5% (151 sachet DAAs with ≥1 packing incident)	1.7 per sachet (250 incidents in 151 sachet DAAs)	
Gilmartin 2015[78] All DAAs (blister pack or sachet)	2389 DAAs	21% (502 DAAs with ≥1 packing incident)	1.5 per DAA (770 incidents, in 502 DAAs)	*DAAs with incidents rated as: Insignificant risk: 138 Minor risk: 273 Moderate risk: 84 Major risk: 93 Catastrophic risk: 6
Gilmartin 2015[78] Blister pack DAAs only	1899 blister pack DAAs	20.6% (391 blister pack DAAs with ≥1 packing incident)	Not reported	
Gilmartin 2015[78] Sachet DAAs only	490 sachet DAAs	22.7% (111 sachet DAAs with ≥1 packing incident)	Not reported	

*Ratings are reported per dose administration aids (DAAs). If separate incidents in the same DAA had different risk ratings, then these were counted once in each risk category. If a DAA had more than one incident in the same risk category, this was reported once in that category.

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