MEDICATION MANAGEMENT IN AGED CARE WHILE MITIGATING COVID-19

POLYPHARMACY

POLYPHARMACY IN AGED CARE

In a review of 176,390 people in aged care facilities in Australia, residents were receiving a median of 11 unique prescription medications, with 62% receiving at least one high-risk medication.[1]

Review of medications by accredited pharmacists and general practitioners identifies a mean of 2.7-3.9 medication-related problems per resident.[1]
A systematic review and meta-analysis of 41 studies that assessed medication reviews intended to reduce inappropriate medication found that the medication reviews:[2]

- reduced overall mortality by 26%
- reduced falls (number of fallers) by 15%, and
- reduced the number of residents with potentially inappropriate medications by 59%.

POLYPHARMACY AND COVID-19 OUTCOMES

Multiple conditions make the elderly population more susceptible to the harmful effects of medication and the deleterious consequences of infections, including COVID-19 (coronavirus).[3]

Polypharmacy is often a proxy for multi-morbidity as many patients with multiple co-morbidities have complex medication regimens. The specific impact of polypharmacy on the relative risk of a positive COVID-19 test, adjusted for number of co-morbidities, was examined for over 400,000 people in the UK Biobank cohort[4]. These authors found that polypharmacy, perhaps a proxy for having multiple chronic conditions, was associated with a dose response for risk of COVID-19 (see **Table 1**).

Number of medications	Relative risk of positive COVID-19 test (95% CI)
0	1 (ref)
1-3	1.13 (0.98-1.31)
4-6	1.58 (1.34-1.87)
7-9	2.24 (1.81-2.77)
10 or more	3.09 (2.37-4.03)

Table 1: Relative risk of positive COVID-19 test by number of regular medications[4]

KEY POINTS

Polypharmacy is associated with an increased risk of contracting COVID-19 infection and with worse outcomes should an infection occur.

Determining whether medications can be omitted, stopped or converted to once-daily formulation is recommended during COVID-19 illness. Many of these changes can be pre-emptively considered.

The use of several centrally acting agents (especially anticholinergic agents) and proton pump inhibitors has been associated with worse clinical outcomes from COVID-19.

While the study above demonstrates an association of polypharmacy with contracting COVID-19, a case-control study in Scotland showed that polypharmacy was also associated with severe COVID-19 outcomes (ICU admission or death).[5] These authors partitioned the drug classes into cardiovascular and non-cardiovascular medications (as it is suggested that cardiovascular medications be considered separately when considering polypharmacy[6]), and examined the number of cases of severe COVID-19 against controls based on the number of non-cardiovascular medications dispensed in the 240 days prior to diagnosis. The results are shown in **Figure 1** and demonstrate that a greater than four-fold increase in severe COVID-19 is associated with 10 or more medications.

The National COVID Clinical Evidence Taskforce has released a clinical flowchart for the management of people with COVID-19 who are older and living with frailty and/or cognitive impairment.[7] **It recommends a review of medication prescriptions to reduce polypharmacy and prevent medicine interactions and adverse events.**[7] Medication reviews assist in optimising the management and clinical control of chronic medical conditions, such as diabetes and COPD, that increase the risk of poor outcomes from COVID-19.[8] Drug interactions are also common in patients with COVID-19. In one study, 55% of patients had a severe drug interaction on admission to hospital with COVID-19.[9]

The National COVID Clinical Evidence Taskforce also points out that in patients with COVID-19, limiting contact – such as providing medications – is important. As such, determining whether medications can be omitted, stopped or converted to a once-daily formulation is recommended during COVID-19 illness.[7]

SPECIFIC MEDICATIONS AND COVID-19 OUTCOMES

The consumption of various commonly used medications can increase the risk and complications of pneumonia and related pulmonary disorders. In the presence of a COVID-19 pandemic, avoiding the use of agents that predispose to pulmonary complications is appropriate.

A review of medications that have adverse pulmonary consequences and are therefore purported to increase the risk of severe COVID-19 was published in April 2020.[10] This list comprised the following:

- antidepressants
- antiepileptic drugs
- antimuscarinic agents
- antipsychotic agents
- drugs used in nausea and vertigo
- gabapentinoids
- gastrointestinal antispasmodics
- H1 antihistamines
- hypnotics and sedatives
- non-steroidal anti-inflammatory agents
- opioid analgesics
- proton pump inhibitors
- urinary antispasmodics.

These theoretical associations were tested in a case-control study undertaken in Scotland.[5] These authors examined associations between consumption of each of these (and other) classes of medications and 'severe' COVID-19 (death or entry to critical care within 28 days of diagnosis). As well as associations with the total number of non-cardiovascular medications (see earlier), the strongest independent associations with specific drug classes were with:

- proton pump inhibitors
- antihistamines
- antipsychotic drugs
- opioid analgesics.

The authors were also able to show a positive dose response relationship for the risk of severe COVID-19 with a greater number of doses (higher doses) of proton pump inhibitors and higher dose of opioids (as oral morphine milligram equivalents).[5]

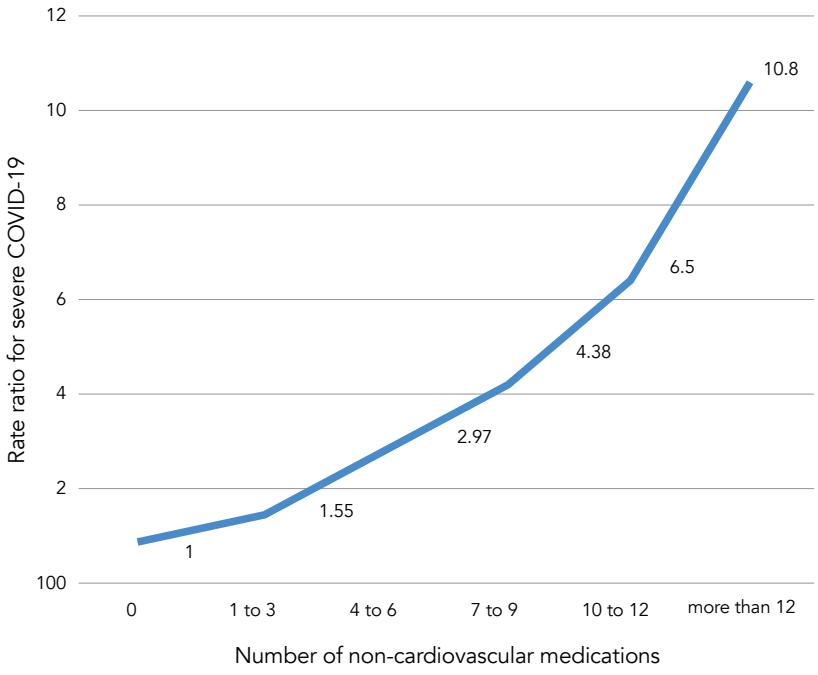

Figure 1: Association of severe COVID-19 with number of non-cardiovascular medications (modified from Reference 5)

PROTON PUMP INHIBITORS

Observational studies suggest that proton pump inhibitor use may predispose people to infection with coronavirus and worse COVID-19 outcomes.

Susceptibility to infection with COVID-19

A nationwide survey in the United States was conducted and multivariable regression analysis found an independent dose-response relationship between the use of proton pump inhibitors and a positive COVID-19 test (see **Table 2**).[11]

As there is evidence that proton pump inhibitors increase the rate of gastrointestinal infections and pneumonia, it is possible that the use of proton pump inhibitors may undermine the gastric barrier to SARS-CoV-2 entry.[11]

Clinical outcomes from COVID-19

A number of observational studies have suggested that proton pump inhibitor use may predispose patients to worse COVID-19 outcomes. Two meta-analyses have collated these studies.[12,13] A total of 12 studies were examined and both meta-analyses concluded that proton pump inhibitor use was associated with an increased risk of developing secondary infections. Since these were published, a Korean study[14] and a study from the United States[15] have also indicated an increase in severe outcomes such as ventilation requirement, ICU admission and death from COVID-19.

PPI exposure	Number in overall cohort (%)	Number in COVID-19 positive cohort (%)	Adjusted odds ratio (95% CI)
No current PPI use	36,583 (68.9)	752 (22.2)	1.0 (ref)
Daily PPI use or less	14,855 (28.0)	2,436 (71.9)	2.15 (1.90-2.44)
Twice daily PPI use	1,692 (3.2)	198 (5.8)	3.67 (2.93-4.60)

Table 2: Proton pump inhibitor use and odds ratio for COVID-19 positive test[11]

MEDICATION MANAGEMENT WHILE MITIGATING COVID-19

Reduce polypharmacy

Taking more medications, especially more psychoactive medications, is associated with worse outcomes in the presence of COVID-19 infection. Pre-emptively reducing the use of all 'less necessary' medications is likely to reduce the number of potential drug interactions and adverse effects, and may improve clinical outcomes should there be a COVID-19 outbreak.

Reduce number of administration times

Reducing the number of contact times during a COVID-19 outbreak can be achieved by reducing the number of administration times for medications which are being used frequently. Many patients in aged care have slower elimination and longer half-lives for common medications such as paracetamol and can have less frequent administration than the younger counterparts. A number of slow-release products are available in multiple therapeutic areas (especially cardiovascular and diabetes) and judicious use of these can reduce the number of administration occasions, thereby reducing close physical contact during a COVID-19 outbreak. Combination products (a large range is available for diabetes and cardiovascular conditions) may similarly reduce medication administration time.

Reduce centrally acting agents, especially anticholinergics

The use of centrally acting agents and respiratory depressants has been shown to worsen outcomes during COVID-19, likely due to their propensity to increase the risk of bacterial pneumonia. Minimising the use of centrally acting agents and respiratory depressants (opioids, antipsychotics, antihistamines and benzodiazepines) is likely to improve outcomes should there be a COVID-19 outbreak.

Delirium is a common presenting complaint for COVID-19 infection in elderly patients and confers a higher risk of poor outcomes in the presence of COVID-19. Although many patients in aged care have co-morbidities that predisposed to delirium, minimising the use of agents that also impact on the frequency of delirium (see delirium guideline) is likely to improve outcomes should there be a COVID-19 outbreak.

Reduce proton pump inhibitors

The use of proton pump inhibitors has been shown in observational studies to increase both the risk of infection with COVID-19 and the likelihood of poor outcomes in the presence of COVID-19. Reducing the use (dose) of these agents, with cessation if possible, is likely to improve outcomes should there be a COVID-19 outbreak.

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