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ORIGINAL RESEARCH ARTICLE

A nationwide study of multimedicine use in people treated with cardiovascular medicines in Australia

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Abstract

Study Objective: Multimorbidity and multimedicine use are common in people with cardiovascular disease and can lead to harms, such as prescribing errors and drug interactions. We quantified multimedicine use in people treated with cardiovascular medicines in a national sample of Australians.

Design: Cross-sectional study.

Data Source: Pharmaceutical dispensing claims for a 10% random sample of Australians.

Patients: Australian adults dispensed any cardiovascular medicine between June and August 2019.

Intervention: None.

Measurements: We quantified the number and type of cardiovascular and non-cardiovascular medicines dispensed during the study period, and the number of unique prescribers, by age and sex.

Main Results: We identified 493,081 people dispensed any cardiovascular medicine (median age = 67 years, 50.2% women). The population prevalence of cardiovascular medicine dispensing increased from 1.7% (n = 10,503) in people 18–34 years to 80.1% (n = 99,271) in people 75–84 years. Cardiovascular medicine dispensing varied by sex; women 18–34 years were more likely to be dispensed any cardiovascular medicine than men (male:female prevalence ratio [PR] = 0.84, 95% confidence interval [CI] = 0.81–0.87), whereas the prevalence of cardiovascular medicine dispensing was higher in men 35–44 years (PR = 1.27, 95% CI 1.24–1.30) and 45–54 years (PR = 1.24, 95% CI 1.22–1.26) and was similar between sexes in people ≥65 years. Overall, both women and men were dispensed a median of 2.0 (interquartile range [IQR] = 1.0–3.0) cardiovascular medicines. Two-thirds of people ≥65 years (73.5%; n = 208,524) were dispensed ≥2 cardiovascular medicines, with 16.6% (n = 6736) of people ≥85 years dispensed five or more. Women and men were dispensed a median of 2.0 (IQR = 1.0–5.0) and 2.0 (IQR = 0.0–4.0) non-cardiovascular medicines, respectively, to treat comorbid conditions, commonly gastroesophageal reflux disease medicines (32.2% of women

and 26.6% of men), antibiotics (28.7% of women and 22.4% of men), and antidepressants (26.3% of women and 15.9% of men). One quarter of both sexes had multiple prescribers for their cardiovascular medicines alone, whereas 54.5% ($n = 134{,}939$) of women and 49.9% ($n = 122{,}706$) of men had multiple prescribers for all medicines.

Conclusion: Multimedicine use is common in people treated with cardiovascular medicines and presents a risk for inappropriate prescribing. Understanding the comorbid conditions commonly treated concurrently with cardiovascular disease can help improve co-prescribing guidelines and develop a person-centered approach to multimorbidity treatment.

KEYWORDS
Australia, cardiovascular disease, multimorbidity, polypharmacy

1 | INTRODUCTION

Cardiovascular disease is the leading cause of disease burden worldwide, and its prevalence has doubled over the past 30 years.[1] In 2017–2018, 1.2 million Australians had a diagnosed cardiovascular condition and 99% of adults have at least one cardiovascular risk factor, such as hypertension or abnormal lipid levels; 57% have three or more risk factors.[2] At all ages, men have higher rates of cardiovascular disease and are also more likely to receive pharmacological treatment than women.[2,3]

Multimorbidity in people with cardiovascular disease is extremely common,[4] as people with one cardiometabolic condition are predisposed to developing another, such as diabetes or chronic kidney disease, because of shared risk factors.[5,6] Non-cardiometabolic conditions such as depression, respiratory disease, and pain are also common in this population for similar reasons.[4] In a 2014 United Kingdom study, one in four people with cardiovascular disease had five or more health conditions.[4] Contemporary Australian data are lacking, but in a 2005 study 99% of people with cardiovascular disease had two or more additional health conditions.[7]

Multimorbidity leads to multimedicine use and polypharmacy, and people taking a large number of medicines are at a higher risk of adverse events, drug–drug interactions, prescribing cascades, and non-adherence.[8,9] In people at risk of cardiovascular disease, many common medicines such as antibiotics, antidepressants, and non-steroidal anti-inflammatory drugs (NSAIDs) may increase the risk of harms including drug-induced hypertension, heart failure, or arrhythmias.[10] In a study of older men, each additional medicine taken (both cardiovascular and/or non-cardiovascular) increased the risk of a cardiovascular event by 9% even after adjusting for comorbidities.[11] Another complicating factor for people with multimorbidity is treatment by multiple health care providers increases the risk of prescribing errors and adverse events.[12] In contrast, guideline-based treatment of people at high risk of cardiovascular disease often requires multiple medicines (one or more antihypertensives, lipid-lowering medicines, antiplatelets, and anticoagulants),[13] and a UK study found that a greater number of cardiovascular medicines actually reduced the risk of unplanned hospital admissions.[14]

A large proportion of older Australians take five or more medicines,[15,16] yet there are no contemporary, population-level Australian data on multimedicine use in people living with or at risk of cardiovascular disease. Understanding common medicine combinations places patients rather than medicines at the center of clinical discussions and guideline development and builds the foundations of research to better understand and differentiate appropriate from inappropriate or problematic polypharmacy.[17] Therefore, our objective was to quantify medicine dispensing in a nationwide, population-based sample of Australian adults treated for cardiovascular disease and its risk factors. Specifically, we (i) estimated the prevalence of dispensing of medicines to treat or prevent cardiovascular disease by age and sex; (ii) quantified the most commonly dispensed medicines to treat comorbid conditions among people dispensed cardiovascular medicines; and (iii) calculated the number of unique prescribers for cardiovascular medicines and non-cardiovascular medicines.

2 | METHODS

2.1 | Context and data source

Australian residents and citizens are eligible for subsidized access to prescribed medicines through the Pharmaceutical Benefits Scheme (PBS). We used PBS dispensing claims for a 10% random sample of all PBS-eligible people; the sample is selected based on the last digit of each person's randomly assigned unique numeric identifier. This is a standard dataset provided by the Australian Government Department of Human Services for analytical use. Our study includes all PBS-listed medicines dispensed in the community, private hospitals, and on discharge from public hospitals in most states. To protect privacy, all dates are offset by up to +14 or −14 days; this offset is the same for each individual. Private dispensings (i.e. medicines not dispensed through the PBS for which the consumer pays the entire cost out-of-pocket) are not captured in these data.

2.2 | Study population

We performed a cross-sectional study of all people aged ≥18 years with one or more dispensings of a cardiovascular medicine between June 1 and August 31, 2019. We chose these 3 months as they are least likely to be affected by seasonal stockpiling.[18] We defined cardiovascular medicines using the same definition as the Australian Institute of Health and Welfare (AIHW)[2] and based on the World Health Organization (WHO) Anatomic Therapeutic Chemical (ATC) classification, and it includes all medicines commonly used to treat or prevent cardiovascular disease or its risk factors.

2.3 | Medicines of interest

Cardiovascular medicines were categorized into classes including: antiarrhythmics, anticoagulants, antiplatelets, beta-blockers, calcium channel blockers, glycosides, lipid modifiers, loop diuretics, potassium-sparing diuretics, renin-angiotensin-aldosterone inhibitors (RAAS), thiazide/thiazide-like diuretics, vasodilators, and other. For some analyses, due to small numbers, antiarrhythmics, glycosides, potassium-sparing diuretics, and vasodilators were also grouped into the "other" category. A full list is shown in Table S1. Non-cardiovascular medicines were categorized into classes based on WHO ATC classes and refined to reflect clinically-relevant categories; a full list is available in Table S2. All medicines were included since even medicines used in the short-term can lead to drug–drug interactions.

When calculating the number of unique medicines, for fixed-dose combinations (FDCs) each component was counted separately (e.g. the combination product atorvastatin + amlodipine counts as two medicines). Thus, from herein "medicine" refers to the number of active ingredients rather than the number of tablets/capsules.

2.4 | Analysis

Consistent with previously used definitions of cumulative polypharmacy,[16,19] the number of unique cardiovascular medicines dispensed for each person in the 3-month study period was calculated. We estimated the population prevalence by class and number of medicines dispensed by age (18–34, 35–44, 45–54, 55–64, 65–74, 75–84, and 85+ years) and sex, using the mid-year Australian Bureau of Statistics (ABS) population as the denominator.[20] Numbers derived from the 10% sample were multiplied by 10 to estimate population-level rates. We identified the most commonly dispensed medicines, and identified combinations based on the classes of unique medicines dispensed within this 3-month period. The most common medicine combinations were visualized using UpSet plots. For the number of medicines dispensed per person, we calculated medians, interquartile ranges, and the mean to better understand the distribution.

The number of non-cardiovascular medicines dispensed to treat comorbid conditions was similarly calculated, as well as the total number of medicines dispensed, within the same 3-month period. The prevalence of each class of non-cardiovascular medicines was measured among people with any dispensing of a cardiovascular medicine, and this prevalence was visualized using heat maps.

The number of unique prescribers per person for cardiovascular and non-cardiovascular medicines was also measured during the study period. We then identified whether cardiovascular medicines and non-cardiovascular medicines were prescribed by the same or different prescribers, and how this varied by medicine class.

2.5 | Ethics approval and data access

The New South Wales Population and Health Services Research Ethics Committee (Reference HREC/13/CIPHS/64) approved the study and the Services Australia External Request Evaluation Committee approved data access.

3 | RESULTS

We identified 493,081 adults dispensed a cardiovascular medicine between June 1 and August 31, 2019. The median age was 67 years (interquartile range [IQR], 57–76 years) and 50.2% were women ($n = 247,446$).

3.1 | Population prevalence of cardiovascular medicine dispensing

The prevalence of cardiovascular medicine dispensing increased with age; 1.7% ($n = 10,503$) of people aged 18–34 years were dispensed one or more cardiovascular medicines, peaking at 80.0% ($n = 99,271$) of people 75–84 years (Table S3). Men aged 18–34 years had a lower prevalence of cardiovascular medicine dispensing than women (1.6% male vs. 1.9% female; male: female prevalence ratio [PR] = 0.84, 95% confidence interval [CI] 0.81–0.87), whereas for people aged 35–64 years, men were more likely to be dispensed a cardiovascular medicine than women, especially those 35–44 years (7.5% male vs. 5.9% female; PR = 1.27, 95% CI 1.24–1.30). Younger men (<65 years) had a higher prevalence of dispensing of most common cardiovascular medicines, specifically RAAS inhibitors, lipid modifiers, thiazide/thiazide-like diuretics, and calcium channel blockers (Figure S1). In contrast, women 18–34 years had a higher prevalence of dispensing of beta-blockers (0.6% female vs. 0.4% male; PR = 0.57, 95% CI 0.50–0.64) and anticoagulants (0.3% female vs. 0.1% male; PR = 0.39, 95% CI 0.27–0.51). The dispensing prevalence rates were more similar between sexes within age groups

in people ≥65 years, with RAAS inhibitors and lipid modifiers dispensed to more than half of Australians ≥75 years (Table S4).

3.2 | Cardiovascular medicine combinations

Among people dispensed cardiovascular medicines, the most common were medicines to treat hypertension and hyperlipidemia. RAAS inhibitors were most dispensed to 65.8% (n = 324,356) of people, followed by lipid-lowering medicines (56.0%, n = 276,243), calcium channel blockers (28.5%, n = 140,260), and beta-blockers (21.6%, n = 106,415; Table S5).

The number of unique cardiovascular medicines dispensed increased with age (Figure 1). Among people aged 18–34 years with any cardiovascular medicine dispensing, 20.2% (n = 2117) were dispensed more than one cardiovascular medicine. Conversely, among people aged 85+ years, more than three-quarters (79.4%; n = 32,274) were dispensed more than one cardiovascular medicine, with 16.6% (n = 6736) dispensed 5 or more. Among people dispensed two or more cardiovascular medicines (n = 316,206), 39.4% were dispensed a fixed-dose combination.

Overall, women and men were dispensed a similar number of unique cardiovascular medicines at all ages, with a median of 2.0 medicines (IQR 1.0–3.0), and a mean of 2.2 and 2.5, respectively (Table S6). This increased with age: both women and men aged 18–34 years were dispensed a median of 1.0 (IQR = 1.0–1.0) cardiovascular medicines (mean = 1.2 and 1.4, respectively), increasing to 3.0 medicines (IQR = 2.0–4.0) in people ≥85 years (mean = 2.9 and 3.0, respectively).

Figure 2 shows the most common cardiovascular medicine combinations. Monotherapy with a RAAS (13%) or lipid modifiers (14%) was most common, followed by a RAAS in combination with a lipid modifier (10%) and a RAAS with a calcium channel blocker (6%). When broken down by age, use of a single cardiovascular medicine class was most common in all age groups except 75–84 years, although this was predominantly beta-blockers in people <35 years, and RAAS or lipid modifiers in older people. In people 75–84 years, the most common combination was a RAAS and a lipid modifier (Figure S2A–G).

3.3 | Dispensing of medicines to treat comorbid conditions

Overall, women were dispensed a median of 2.0 (IQR 1.0–5.0) and men were dispensed a median of 2.0 (IQR 0.0–4.0) non-cardiovascular medicines (mean = 3.2 and 2.6, respectively). This ranged from a median of 2.0 (IQR 1.0–4.0; mean = 2.7) in women and 1.0 (IQR 0.0–3.0; mean = 1.9) in men aged 18–34 years, to a median of 4.0 (IQR 2.0–6.0; mean = 4.1) in women and 3.0 (IQR 2.0–6.0; mean = 3.2) in men aged 85+ years (Figure 3, Table S6). One fifth (21.6%; n = 106,513) of people were not dispensed any non-cardiovascular medicines; this was highest in people 18–34 years (25.9%; n = 2723) and lowest in people 85+ years (8.9%; n = 3609). Over one third (37.4%; n = 15,192) of people 85+ years were dispensed 5 or more non-cardiovascular medicines. Considering all medicines combined, women were dispensed a median of 5.0 medicines (IQR 3.0–7.0; mean = 5.4), whereas men were dispensed a median of 4.0 (IQR 2.0–7.0; mean = 5.1).

The most common non-cardiovascular medicines varied by age and sex. Antibiotics and antidepressants were commonly dispensed across all ages and sexes; antibiotics were dispensed to 28.7% (n = 70,971) of women and 22.4% (n = 55,044) of men, whereas antidepressants were dispensed to 26.3% (n = 65,197) of women and 15.9% (n = 39,170) of men and NSAIDs to 10.5% (n = 25,914) of women and 8.7% (n = 21,339) of men. Among people <35 years, opioids were also commonly dispensed (17.4% in women and 10.3% in men), whereas younger women had high rates of dispensing of sex hormones (primarily birth control; 20.4% in women and 2.0% in men aged 18–34 years; Figure 4; Table S7). Among older people, medicines to treat GERD were most common, dispensed to 45.4% (n = 11,256) of women and 43.5% (n = 6892) of men aged ≥85 years.

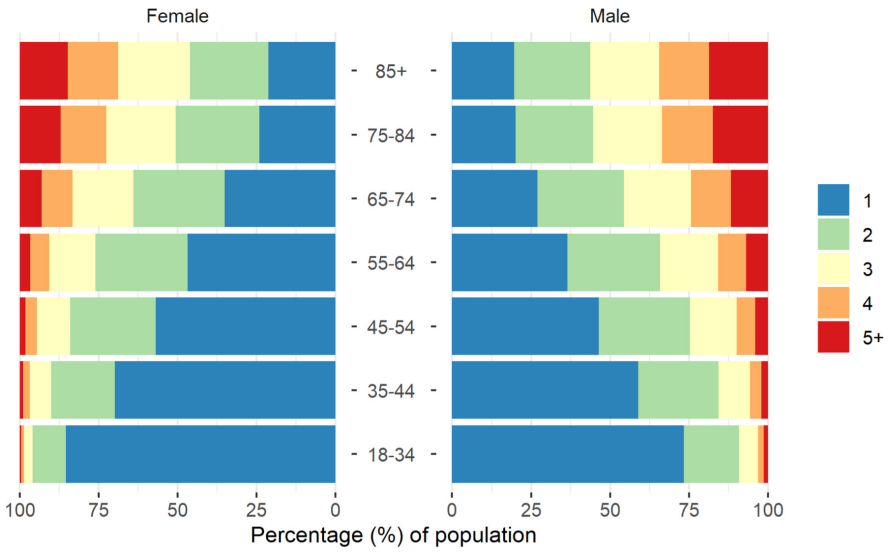

FIGURE 1 Number of unique cardiovascular medicines dispensed by age and sex among people dispensed one or more cardiovascular medicines (n = 493,081).

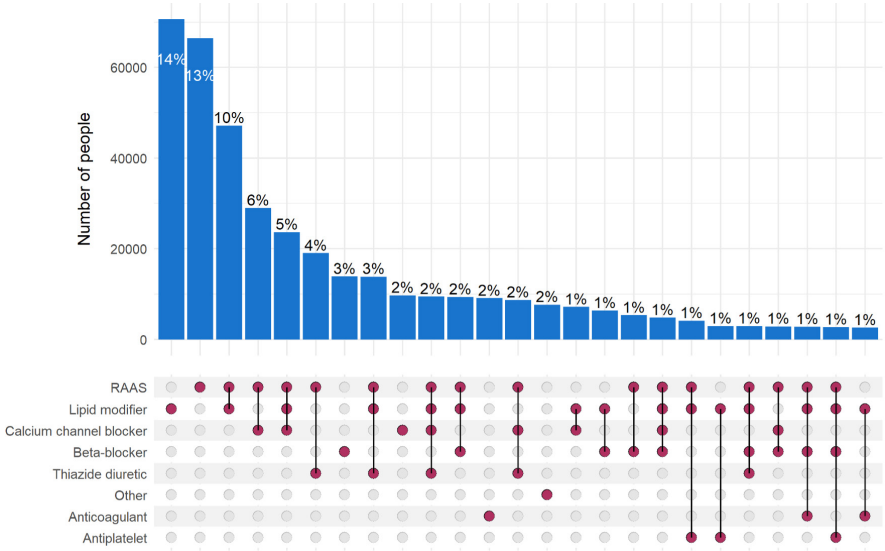

FIGURE 2 Most common combinations of cardiovascular medicine classes (n = 493,081).

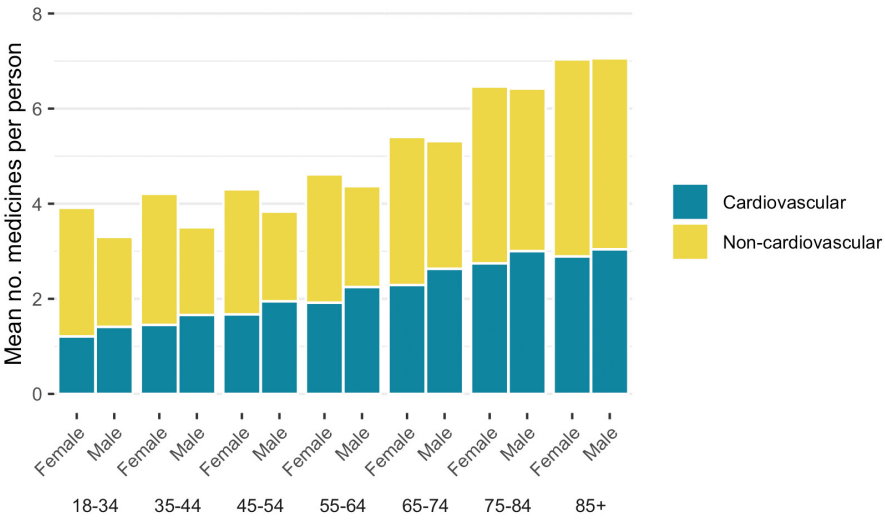

FIGURE 3 Mean number of unique cardiovascular and non-cardiovascular medicines dispensed among people dispensed one or more cardiovascular medicines by age and sex (n = 493,081).

Dispensing of medicines to treat diabetes ranged from 9.2% (n = 523) in women and 9.6% (n = 464) in men aged 18–34 years and peaked at 16.9% (n = 12,109) of women and 22.6% (n = 16,246) of men aged 65–74 years.

3.4 | Number of prescribers

The median number of prescribers of cardiovascular medicines per person was 1.0 in women (IQR 1.0–1.0; mean = 1.3) and 1.0 in men (IQR 1.0–2.0; mean = 1.3); median number of prescribers for all medicines per person was 2.0 (IQR 1.0–2.0; mean = 1.9) in women and 1.0 (IQR 1.0–2.0; mean = 1.8) in men. One quarter of women (24.6% [n = 60,790]) and men (25.5% [n = 62,732]) had multiple prescribers for their cardiovascular medicines.

Considering all medicines, 54.5% (n = 134,939) of women and 49.9% (n = 122,706) of men had two or more prescribers, 23.8% (n = 58,773) of women and 20.4% (n = 49,991) of men had three or more prescribers, and 9.6% (n = 23,830) of women and 8.1% (n = 19,854) of men had four or more prescribers during the 3-month study period. Immunosuppressants (e.g. disease-modifying antirheumatic drugs [DMARDs] to treat autoimmune conditions, 70.2%) and cancer medicines (58.7%) were commonly prescribed by a different prescriber from cardiovascular medicines, as were antibiotics (50.2%) and opioids (42.9%; Figure 5).

4 | DISCUSSION

This study presents contemporary, population-level information on patterns of cardiovascular multimedicine use across the Australian population. We found that use of multiple cardiovascular medicines was very common, as was use of multiple medicines to treat comorbid conditions—which were often prescribed by multiple prescribers. We also found differences by age and sex, which reflect known treatment patterns of cardiovascular disease,[2,3,21] yet may also reflect areas of potential inefficiency in prescribing. For example, in younger people we observed greater use of beta-blockers

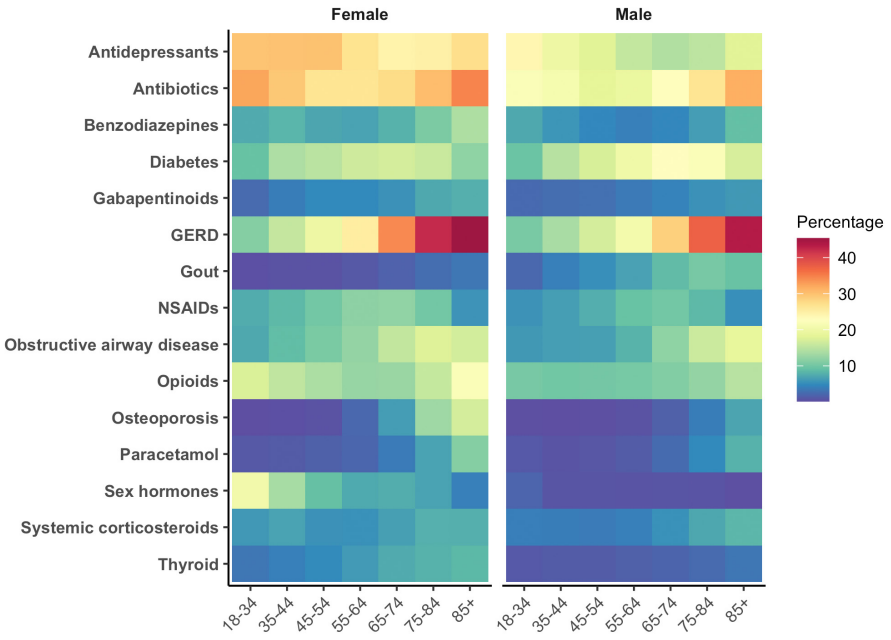

FIGURE 4 Prevalence of the 15 most common non-cardiovascular oral medicine classes by age group and sex. Red indicates a higher prevalence, and blue a lower prevalence. GERD, gastro-esophageal reflux disease; NSAIDs, non-steroidal anti-inflammatory drugs.

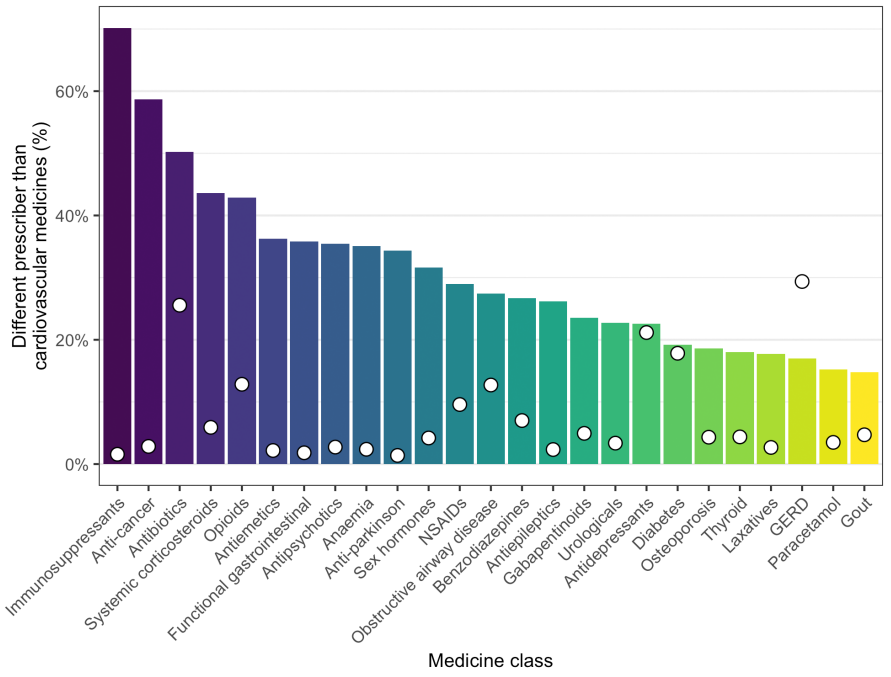

FIGURE 5 The proportion of people dispensed a class of non-cardiovascular medicines, for whom the prescriber of this medicine was different to that of the cardiovascular medicines. The white dots represent the percentage of the study population dispensed that medicine class.

in women than men, which may be due to contraindications of the most common first-line antihypertensive (angiotensin-converting enzyme inhibitors) in pregnancy[22] or off-label use for migraine or social anxiety. Antidepressant use in young people treated with cardiovascular medicines was also higher than in the general population,[23] potentially related to the cardiometabolic effects of mental health disorders and the medicines used to treat them.[24,25] Our findings highlight the need for ongoing monitoring of pharmacotherapy in patients with cardiovascular disease, as well as the need for co-guidelines on prescribing for treatment of multimorbid conditions.

Many studies have identified an increased risk of harms associated with polypharmacy, which is typically defined as five or more medicines.[26] A dichotomous definition of polypharmacy is limited, as adequate treatment and prevention of cardiovascular disease in high-risk individuals often requires multiple pharmacological agents; for instance, there is growing evidence that more intensive blood pressure control with up to three antihypertensives improves outcomes.[27,28] One study of 181,000 people found that cardiovascular polypharmacy was associated with a decreased risk of unplanned hospitalization even after adjusting for confounding.[14]

Although we did not have diagnosis information, we found high rates of dispensing of medicines that would increase the risk of poor cardiovascular health, such as antidepressants[25] (dispensed to 26% of women and 16% of men) and NSAIDs (dispensed to 11% of women and 9% of men),[29] suggesting inappropriate prescribing may be high. NSAIDs are associated with multiple drug–drug interactions; when

combined with RAAS inhibitors and diuretics, they increase the risk of impaired renal function, and NSAIDs combined with anticoagulants increase the risk of bleeding.[29,30] Non-cardiovascular medicines impact cardiovascular health not only via drug interactions but also by acting directly on the cardiovascular system. A United States study found that 19% of adults with hypertension were dispensed medicines known to raise blood pressure (e.g. antidepressants and NSAIDs), which was associated with a greater risk of uncontrolled hypertension.[31]

Although medicine classes like antipsychotics and antiepileptics that increase the risk of metabolic syndrome (obesity, hypertension, hyperlipidemia, and insulin resistance)[32] were not common, more concerning is the large number of non-cardiovascular medicines that people were dispensed. Even if the risk associated with an individual medicine is small, each additional medicine with known cardiovascular adverse effects that a person is exposed to increases the risk of myocardial infarction, stroke, and death in a dose–response fashion, with certain combinations (e.g. antidepressants + opioids) identified as being particularly harmful.[33] When assessing a patient's cardiovascular risk, it is important to consider the cardiovascular safety of all of a patient's medicines, including both the cumulative burden and potential interactions. Where they exist, alternative treatments with better cardiac safety profiles should be considered (e.g. selective serotonin reuptake inhibitors instead of tricyclic antidepressants for depression), although this is not always feasible. For instance, although NSAIDs carry risks, opioids have also been associated with cardiovascular harms, as well as the risk of tolerance and dependence, leaving few alternatives for pain relief.[29]

Although not unexpected, medicines for non-cardiovascular conditions were more likely to be prescribed by different prescribers, especially medicines often prescribed by specialists (e.g. cancer medicines). A greater number of practitioners is associated with an increased risk of suboptimal prescribing,[34] adverse events,[12] and poor adherence.[35,36] People with multimorbidity frequently receive care from multiple providers ("fragmented care") creating a challenge in optimizing pharmacological treatment, with many prescribing errors occurring due to poor coordination between providers and inaccurate recording of medicines.[37] One concerning finding in our study is that opioids (dispensed to 11% of men and 15% of women) were often prescribed by a different prescriber to a person's cardiovascular medicines. Recent studies have linked a greater risk of adverse cardiovascular events in people taking opioids,[38] especially when taken in combination with NSAIDs, antidepressants, or bronchodilators.[33] Even if different providers all follow best practice guidelines, prescribing recommendations for various conditions can clash. A 2015 study found that UK treatment guidelines rarely consider people with multimorbidity and identified 111 potential interactions between medicines recommended in heart failure and common comorbidities that increase the risk of cardiovascular harms such as hypotensive effects, bradycardia, and arrhythmias.[39]

Our work highlights the high prevalence of multimedicine use in people treated for cardiovascular disease, and thus the need for strategies to reduce harms resulting from drug–drug interactions and use of medicines contraindicated in people with cardiovascular disease. A person-centered (rather than disease-centered) approach for people with multimorbidity is recommended, which considers individuals' needs and priorities to minimize treatment burden and complexity.[40] Although such an approach can be difficult to implement in practice,[41] uptake can be facilitated through health professional training,[42] clinical guidelines that take into account multimorbidity,[43] and centralized electronic prescribing tools.[42] An example of such a strategy is comprehensive medication management (CMM),[44,45] involving pharmacists working with patients to optimize their medicine use by identifying, resolving, and preventing medicine-related problems; a small trial of CMM demonstrated improvements in clinical outcomes and reductions in unplanned health service utilization in people with cardiovascular disease.[46]

Further research examining longitudinal patterns of medicine use will support a better understanding of the drivers of polypharmacy, overprescribing, and inappropriate medicine use. Prescribing cascades, where a second medicine is administered in response to an adverse effect from another medicine, have been identified with several cardiovascular medicines, such as calcium channel blockers and loop diuretics[47] and NSAIDs and antihypertensives[48] and may represent one potential point of intervention.

4.1 | Strengths and limitations

This is a nationwide, population-based study representative of all Australians. We have considered all medicines, prescribed for chronic and acute conditions, to better understand all medicines being used in our study population. We used data from 2019, which are likely to be more representative of typical practice in Australia than at the height of the COVID-19 pandemic, which experienced disruptions due to medicine stockpiling, drug shortages, and changes in interactions with the health care system. We have not attempted to determine appropriateness of prescribing, but rather to quantify the extent of medicine use in this population at risk of potential adverse events. Similarly, we did not have information on the indication for prescribing, and could not distinguish between cardiovascular medicines used for primary or secondary prevention. Some cardiovascular medicines may also be used off-label to treat non-cardiovascular conditions, such as beta-blockers like propranolol used for migraines, especially in young women. Although we could not identify people with cardiovascular disease not treated with medicines, 79% of Australians with cardiovascular disease are treated pharmacologically.[2] Over-the-counter medicines and medicines dispensed in public hospitals are also not captured in the data collection used in this study; notably, over-the-counter NSAIDs (e.g. ibuprofen) which as we have highlighted as being potentially problematic. Lastly, we have described medicine use in a 3-month window; although this definition has been used previously to define polypharmacy and therapeutic

complexity,[16,19,36] as with all studies using dispensing data we do not know if medicines were definitively used concurrently or even taken at all.

5 | CONCLUSION

We have identified that multimedicine use is common in people treated with cardiovascular medicines, and strategies are needed to avoid issues arising from drug–drug interactions or inappropriate prescribing such as an increased risk of adverse reactions and poor compliance. Further research is needed to better understand gaps between the most common conditions being treated concurrently with cardiovascular disease and existing clinical guidelines to help improve co-guidelines on prescribing.

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CONFLICT OF INTEREST

The Centre for Big Data Research in Health, UNSW received funding from Abbvie in 2020 for work unrelated to this manuscript.

DATA AVAILABILITY STATEMENT

Restrictions apply to availability of these data, which were used under license for this study. Access to these data by other individuals or authorities is not permitted without the express permission of the approving human research ethics committees and data custodians. Interested parties may request access to the data by contact Australian Government Services Australia (https://www.servicesaustralia.gov.au/statistical-information-and-data).

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SUPPORTING INFORMATION

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

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