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ORIGINAL ARTICLE

Medications and cognitive risk in Aboriginal primary care: a cross-sectional study

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Key words
polypharmacy, suboptimal prescribing, anticholinergic burden, cognitive risk.

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Abstract

Background: Aboriginal and Torres Strait Islander people are ageing with high rates of comorbidity, yet little is known about suboptimal prescribing in this population.
Aim: The prevalence of potentially suboptimal prescribing and associated risk factors were investigated among older patients attending primary care through Aboriginal Community Controlled Health Services (ACCHSs).
Methods: Medical records of 420 systematically selected patients aged ≥50 years attending urban, rural and remote health services were audited. Polypharmacy (≥ 5 prescribed medications), potentially inappropriate medications (PIMs) as per Beers Criteria and anticholinergic burden (ACB) were estimated and associated risk factors were explored with logistic regression.
Results: The prevalence of polypharmacy, PIMs and ACB score ≥3 was 43%, 18% and 12% respectively. In multivariable logistic regression analyses, polypharmacy was less likely in rural (odds ratio (OR) = 0.43, 95% confidence interval (CI) = 0.24–0.77) compared to urban patients, and more likely in those with heart disease (OR = 2.62, 95% CI = 1.62–4.25), atrial fibrillation (OR = 4.25, 95% CI = 1.08–16.81), hypertension (OR = 2.14, 95% CI = 1.34–3.44), diabetes (OR = 2.72, 95% CI = 1.69–4.39) or depression (OR = 1.91, 95% CI = 1.19–3.06). PIMs were more frequent in females (OR = 1.88, 95% CI = 1.03–3.42) and less frequent in rural (OR = 0.41, 95% CI = 0.19–0.85) and remote (OR = 0.58, 95% CI = 0.29–1.18) patients. Factors associated with PIMs were kidney disease (OR = 2.60, 95% CI = 1.37–4.92), urinary incontinence (OR = 3.00, 95% CI = 1.02–8.83), depression (OR = 2.67, 95% CI = 1.50–4.77), heavy alcohol use (OR = 2.83, 95% CI = 1.39–5.75) and subjective cognitive concerns (OR = 2.69, 95% CI = 1.31–5.52). High ACB was less common in rural (OR = 0.10, 95% CI = 0.03–0.34) and remote (OR = 0.51, 95% CI = 0.25–1.04) patients and more common in those with kidney disease (OR = 3.07, 95% CI = 1.50–6.30) or depression (OR = 3.32, 95% CI = 1.70–6.47).
Conclusion: Associations between potentially suboptimal prescribing and depression or cognitive concerns highlight the importance of considering medication review and deprescribing for these patients.

Abbreviations: ACB, anticholinergic cognitive burden; ACCHS, Aboriginal Community Controlled Health Service; ACE, angiotensinogen-converting enzyme; CI, confidence interval; CNS, central nervous system; COX, cyclooxygenase; IQR, interquartile range; NS, not significant; NSAID, non-steroidal anti-inflammatory drug; OR, odds ratio; PIM, potentially inappropriate medication

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Introduction

Aboriginal and Torres Strait Islander people experience disproportionately high rates of multimorbidity with chronic diseases such as cardiovascular disease, chronic kidney disease and dementia emerging at a younger age than the general Australian population.[1,2] Disparities in

social determinants of health and the negative effects of racism and intergenerational trauma stemming from colonisation are thought to contribute to many of these inequitable health outcomes.[3]

To address this disparity, Aboriginal primary healthcare services are delivered at more than 300 locally operated Aboriginal Community Controlled Health Services (ACCHSs) across the country. These services aim to improve health outcomes by delivering culturally appropriate and holistic community and health services.[4] A key function of these organisations is to ensure safe and appropriate medication use, as there are multiple challenges associated with maintaining safe prescribing in Aboriginal primary care. These challenges include ubiquitous issues such as suboptimal prescribing and poor communication between care team members and patients, in addition to specific cultural and patient-related factors.[5]

Potentially suboptimal prescribing for older people may involve polypharmacy (the concurrent use of ≥5 medications), the use of potentially inappropriate medications (PIMs) and underprescribing of indicated medications.[6] Polypharmacy is associated with falls, functional disability, frailty and adverse outcomes for older men and women.[7,8] Polypharmacy affects over a third of older people aged ≥70 years in the general Australian population,[9] and half of older community-dwelling Aboriginal and Torres Strait Islander adults.[10,11]

PIMs are documented in approximately half the population over 70 years and include high-risk medications and/or concurrent medications that often lead to a prescribing cascade.[12–14] Medications commonly considered to be PIMs include those with strong anticholinergic effects, such as tricyclic antidepressants and incontinence medications, that are associated with cognitive decline and functional impairment over time.[15] The effects of less potent anticholinergics are thought to be cumulative,[16] and measures such as the anticholinergic cognitive burden (ACB) scale estimate this burden. Important limitations of standardised medication assessments in differentiating between appropriate and inappropriate prescribing in diverse clinical contexts are highlighted elsewhere.[17]

Suboptimal prescribing, including polypharmacy, and ACB among Aboriginal and Torres Strait Islander peoples were investigated in two recent studies.[10,11] In remote communities, one in five people were using PIMs,[10] while approximately half in regional/urban communities were taking anticholinergic medications.[11] However, these studies were undertaken in only two regions with vast geographical separation, and the situation in other areas of Australia is unknown. Further work is required to clarify the prevalence of polypharmacy and suboptimal prescribing among Aboriginal and Torres Strait Islander peoples with respect to cognitive impairment and dementia risk.

This study aimed to define the prevalence of polypharmacy, PIMs and ACB among Aboriginal and Torres Strait Islander people aged ≥50 years attending ACCHSs in urban, rural and remote areas in Victoria and Western Australia. Associations between polypharmacy, PIMs, ACB and health characteristics, including multimorbidity and cognitive impairment, were assessed.

Methods

Study design

The Let's CHAT (Community Health Approaches To) Dementia in Aboriginal and Torres Strait Islander Communities project involves the co-design and implementation of a culturally responsive best practice model of dementia care in Aboriginal primary care.[18] This study is a nested cross-sectional study utilising Let's CHAT Dementia baseline and additional medication data collected for a subset of ACCHSs (Fig. 1).

Baseline audits of electronic medical records at co-researching ACCHSs were completed for eligible patients. This captured information about patients' dementia risk profile, assessments and investigations relating to cognition (including whether the patients themselves, their family members and/or practice staff had raised concerns about their memory or thinking) and new diagnoses of dementia and cognitive impairment over 6 months from 1 September 2018 or 1 October 2018, until 28 February 2019 or 31 March 2019, dependent on the ACCHS. Additional audits, conducted retrospectively by author MH, captured prescription medications and comorbidities documented over the same period. MH undertook this work as part of her Doctor of Medicine/Master of Public Health studies. Medication data were matched to baseline data using patients' unique identification codes. The Charlson Comorbidity Index was generated for patients to describe comorbidities in relation to life expectancy, excluding a single criterion about HIV status because that information was unavailable.[19] All data were deidentified and stored on a secure digital platform, REDCap.

Three ACCHSs, two from urban and rural Victoria and one from Western Australia (remote), were invited to participate in medication audits based on geographical setting, use of an electronic medical record (EMR) system, capacity to have audits performed remotely during COVID-19 public health restrictions and a strong relationship with the project. Records met eligibility criteria if patients were active (≥3 visits within 2 years),

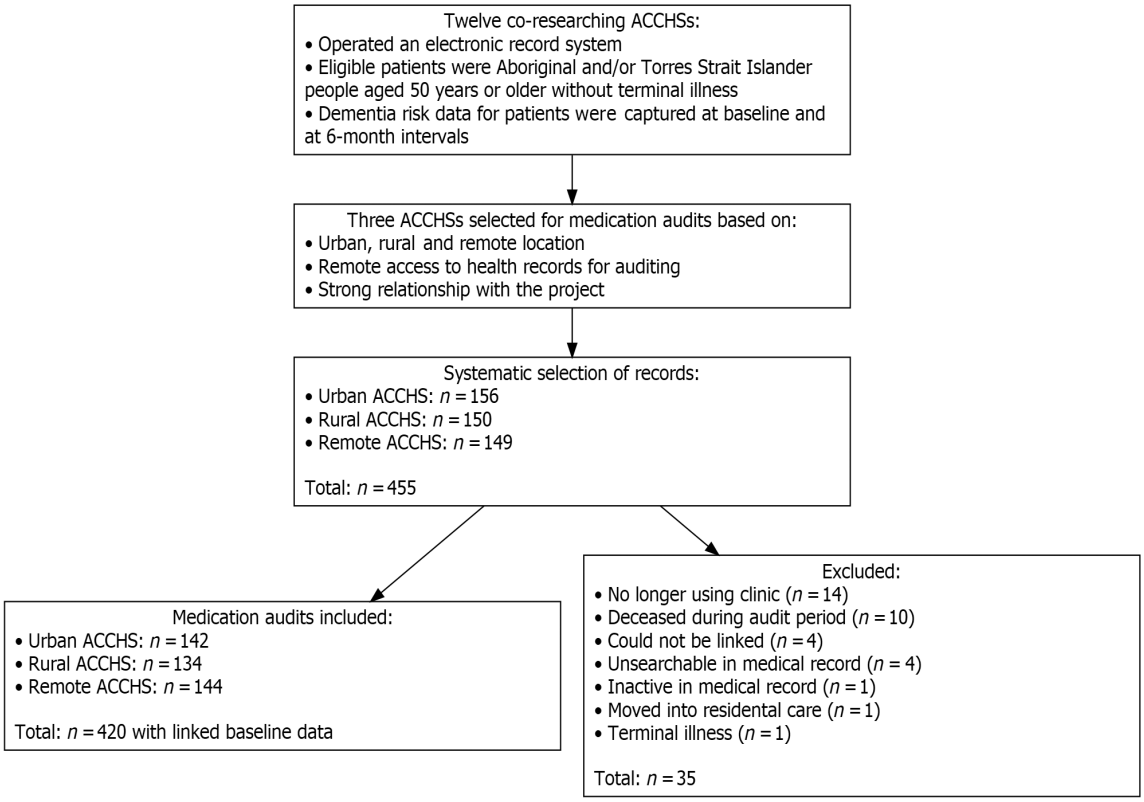

Figure 1 Summary of co-researching Aboriginal Community Controlled Health Services (ACCHSs) and patient records included in the study.

documented as Aboriginal or Torres Strait Islander, aged ≥50 years and without terminal illness at baseline (Fig. 1). We wanted to estimate the prevalence of polypharmacy (our primary factor of interest) with a margin of error of no more than 5%, with a 95% confidence interval (CI). Based on an assumed prevalence of 53% given previous work,[10] this required a sample size of 382 people. The baseline dataset included around 150 patients from each health service, which comfortably met the requirement. Audit lists for the baseline dataset were generated by systematically sampling patients from an alphabetical list, whereby the sample interval was defined by dividing the size of the population (N) by the size of the sample (n). For example, if $N = 600$ in one health service, the sample interval was 4, and every fourth person on the alphabetical list was audited. A total of 455 records were identified.

Medications and potentially suboptimal prescribing

The EMR interfaces used by the practices were MMEx, Communicare and Best Practice. Medication data were retrieved from the medications section of each EMR, which were maintained by practice staff, primarily including general practitioners (GPs) practice nurses and Aboriginal and /or Torres Strait Islander Health Workers and Health Practitioners (AHW/Ps). The patient name, dose, frequency, mode of administration and date of prescription were recorded for each medication prescribed. Medications were then coded according to the Anatomical Therapeutic Chemical (ATC) classification system.[20] Medications containing ≥2 pharmacological agents were recorded using a single ATC combination code. Medications prescribed for a period shorter than 4 weeks or *pro re nata* (as needed) were categorised as 'PRN', as distinguished from 'regular' medications taken over a longer period. PRN medications were included since some anticholinergic medications (such as opiates and sedatives) are often taken on a PRN basis.

Criteria to detect polypharmacy and PIMs and the ACB scale were used to define the prevalence of potentially suboptimal prescribing. Polypharmacy was defined as ≥5 PRN or regular medications prescribed within the audit period. The 2019 Beers Criteria were used to define PIMs, including drug–disease and drug–drug interactions.[12] As a result of data limitations, criteria dependent on diagnostic markers such as renal function, and some disease states or syndromes were excluded. Taking a conservative approach, criteria

defining medications to be used with caution were also excluded. Criteria included in this study are listed in Table 3.

Anticholinergic medications were identified from published literature and the *Australian Medicines Handbook*.[21–24] Each medication received a score according to its anticholinergic effect, as per the ACB scale: medications with affinity for muscarinic receptors or weak anticholinergic effects were assigned a score of 1, and those with marked anticholinergic effects were assigned a score of 2 or 3 (Table S1). Medications with no anticholinergic effects were scored 0. Each patient was assigned an overall ACB score by summing the scores.

Statistical analysis

Data were analysed using the Stata statistical package, version 16 (StataCorp, College Station, TX, USA). After excluding patients who did not meet inclusion criteria, 420 records were retained for analysis (Fig. 1). We used the Kruskal–Wallis equality-of-populations rank test and Pearson's chi-squared test to assess differences between patients' demographic characteristics, cognitive risk factors and potentially suboptimal prescribing across ACCHSs. Binary logistic regression was used to explore factors associated with polypharmacy, one or more PIMs, having ACB score ≥ 1 and having ACB score ≥ 3. All variables which were significant in univariable analyses were entered into multivariable models, after which we removed non-significant covariates in a manual, backwards manner. We retained non-significant covariates in models where clinical judgement dictated this was appropriate, unless model fit was substantially worsened. We used Hosmer and Lemeshow's goodness-of-fit test and the Akaike and Bayesian information criterion to ensure appropriate model fit. Because data for cognition were missing for a small proportion of participants (2.9%), we handled the issue of missing data by

Table 1 Characteristics of Aboriginal and Torres Strait Islander patients across three ACCHSs

	Entire sample	Urban ACCHS	Rural ACCHS	Remote ACCHS	
	Median (IQR) or *n* (% of patients)	Median (IQR) or *n* (% of patients)	Median (IQR) or *n* (% of patients)	Median (IQR) or *n* (% of patients)	*P* value
Age (years)	58 (54–64)	59 (54–64)	57 (53–63)	58 (55–66)	0.154
Ethnicity					**<0.001**
Aboriginal	406 (96.7)	131 (92.2)	133 (99.2)	142 (98.6)	
Torres Strait Islander	2 (0.5)	0 (0)	0 (0)	2 (1.4)	
Aboriginal and Torres Strait Islander	12 (2.9)	11 (7.8)	1 (0.8)	0 (0)	
Sex					0.274
Male	196 (46.7)	62 (43.7)	59 (44.0)	75 (52.1)	
Female	224 (53.3)	80 (56.3)	75 (56.0)	69 (47.9)	
Attended clinic in last 6 months	329 (78.3)	113 (79.6)	103 (76.9)	113 (78.5)	0.860
Charlson Comorbidity Index	3 (2–5)	3 (1–5)	2 (2–4)	3 (2–6)	**<0.001**
Medical conditions					
Heart disease	147 (35.0)	34 (23.9)	46 (34.3)	67 (46.5)	**<0.001**
Atrial fibrillation	16 (3.8)	3 (2.1)	4 (3.0)	9 (6.3)	0.157
Hypertension	214 (51.0)	60 (42.3)	74 (55.2)	80 (55.6)	**0.039**
Diabetes	155 (36.9)	37 (26.1)	54 (40.3)	64 (44.4)	**0.003**
Kidney disease	94 (22.4)	20 (14.1)	16 (11.9)	58 (40.3)	**<0.001**
Stroke	35 (8.3)	13 (9.2)	12 (9.0)	10 (6.9)	0.757
Urinary incontinence	19 (4.5)	13 (9.2)	3 (2.2)	3 (2.1)	**0.005**
Previous of head injury	21 (5.0)	4 (2.8)	10 (7.5)	7 (4.9)	0.208
History of depression	159 (37.9)	70 (49.3)	46 (34.3)	43 (29.9)	**0.002**
Currently smoking	196 (46.7)	70 (49.3)	67 (50.0)	59 (41.0)	0.238
Current heavy alcohol user	75 (17.9)	14 (9.9)	17 (12.7)	44 (30.6)	**<0.001**
Concerns about cognition† (11 missing)	48 (11.4)	15 (10.6)	16 (11.9)	17 (11.8)	0.859
Identified cognitive impairment (12 missing)	15 (3.6)	3 (2.1)	6 (4.5)	6 (4.2)	0.471
Total medications	3 (0–8)	4 (0–8)	2 (0–6)	5 (0–12)	**<0.001**
Taking ≥1 medication	294 (70.0)	103 (72.5)	88 (65.7)	103 (71.5)	0.409
Polypharmacy (≥5 medications)	182 (43.3)	60 (42.3)	43 (32.1)	79 (54.9)	**0.001**
Taking ≥1 PIM	74 (17.6)	34 (23.9)	14 (10.5)	26 (18.1)	**0.013**
ACB ≥1	161 (38.3)	73 (51.4)	38 (28.4)	50 (34.7)	**<0.001**
ACB ≥3	50 (11.9)	28 (19.7)	3 (2.2)	19 (13.2)	**<0.001**

†Concerns about memory or thinking problems.

ACB, anticholinergic cognitive burden; ACCHS, Aboriginal Community Controlled Health Service; IQR, interquartile range; PIM, potentially inappropriate medication.

P values are for Person's chi-square or Kruskal–Wallis equality-of-populations rank test. Bold indicates statistical significance ($P < 0.05$).

Table 2 Univariable and multivariable analysis of factors associated with polypharmacy and potentially inappropriate medications (PIMs)

	Polypharmacy				PIMs ≥ 1			
	Univariable		Multivariable†		Univariable		Multivariable†	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age (years)	1.06 (1.03–1.09)	**<0.001**	1.03 (1.00–1.06)	0.070	1.02 (0.99–1.05)	0.154	1.02 (0.98–1.06)	0.323
Female sex	1.31 (0.89–1.93)	0.172	‡		1.78 (1.06–3.00)	**0.030**	1.88 (1.03–3.42)	**0.040**
Health service								
Urban	1	**<0.001**	1	**0.002**	1	0.016	1	**0.049**
Rural	0.65 (0.39–1.06)		0.43 (0.24–0.77)		0.37 (0.19–0.73)		0.41 (0.19–0.85)	
Remote	1.66 (1.04–2.65)		1.15 (0.66–1.98)		0.70 (0.39–1.24)		0.58 (0.29–1.18)	
Medical conditions								
Heart disease	3.73 (2.45–5.68)	**<0.001**	2.62 (1.62–4.25)	**<0.001**	1.43 (0.86–2.39)	0.172	‡	
Atrial fibrillation	6.03 (1.69–21.47)	**0.005**	4.25 (1.08–16.81)	**0.039**	2.21 (0.74–6.55)	0.154	‡	
Hypertension	3.23 (2.15–4.84)	**<0.001**	2.14 (1.34–3.44)	**0.002**	1.62 (0.70–1.92)	0.557	‡	
Diabetes	3.70 (2.44–5.62)	**<0.001**	2.72 (1.69–4.39)	**<0.001**	1.38 (0.83–2.30)	0.214	‡	
Kidney disease	3.53 (2.18–5.74)	**<0.001**	NS		2.58 (1.50–4.44	**0.001**	2.60 (1.37–4.92)	**0.003**
Stroke	2.72 (1.32–5.64)	**0.007**	NS	**0.023**	1.19 (0.50–2.83)	0.700	‡	
Urinary incontinence	2.97 (1.11–7.98)	**0.030**	NS		4.65 (1.82–11.90)	**0.001**	3.00 (1.02–8.83)	**0.046**
Previous head injury	1.47 (0.61–3.53)	0.393	‡		1.49 (0.53–4.22)	0.448	‡	
History of depression	1.51 (1.02–2.25)	**0.041**	1.91 (1.91–3.06)	**0.007**	2.95 (1.76–4.93)	**<0.001**	2.67 (1.50–4.77)	**0.001**
Current smoker	0.56 (0.38–0.82)	**0.003**	NS		1.34 (0.81–2.22)	0.252	‡	
Heavy alcohol use	1.03 (0.62–1.71)	0.898	‡		1.79 (0.99–3.24)	0.055	2.83 (1.39–5.75)	**0.004**
Concerns about cognition§	1.73 (0.94–3.17)	0.077	‡		3.27 (1.71–6.26)	**<0.001**	2.69 (1.31–5.52)	**0.007**
Identified cognitive impairment	1.45 (0.52–4.09)	0.478	‡		2.35 (0.78–7.09)	0.130	‡	

†This column includes ORs only for age and other variables with statistically significant associations in a final multivariable model. Other variables with statistically significant associations in univariable analysis did not reach statistical significance in the initial multivariable modelling and were excluded from the final multivariable model.

‡Variable not considered in multivariable modelling as did not reach statistical significance in univariable analysis.

§Concerns about memory or thinking problems.

CI, confidence interval; NS, not significant; OR, odds ratio.

Bold = statistically significant result ($P < 0.05$).

performing complete case analysis. We considered *P* values <0.05 statistically significant.

Ethics

Organisational consent was sought from ACCHSs for data collection about cognitive impairment outcomes and medications. Specific permission was obtained from ACCHSs to complete medication audits remotely. Ethics approval was granted from the Aboriginal Health and Medical Research Council Ethics Committee (reference numbers: 1362/18 and 1855/21), the Western Australian Aboriginal Health Ethics Committee (reference number: 858) and The University of Melbourne Medicine and Dentistry Human Ethics Sub-Committee (IDs: 1851943 and 12140).

Results

The median age of patients was 58 years (interquartile range (IQR): 54–64), and the majority identified as Aboriginal (96.7%) and were female (53.3%). Across ACCHSs, patients had similar age, sex and attendance status. The prevalence of several documented chronic conditions and cognitive risk factors varied across health services (Table 1).

The majority of patients were prescribed at least one medication (70.0%), with 43.3% (95% CI = 38.7–48.1%) exposed to polypharmacy. The prevalence of polypharmacy differed significantly between locations, ranging from 32.1% at the rural ACCHS to 54.9% at the remote ACCHS. Heart disease, atrial fibrillation, hypertension, diabetes and depression were associated with greater odds of polypharmacy (Table 2).

Overall, 17.6% of patients (95% CI = 14.3–21.6%) were prescribed one or more PIMs, with lower odds for rural and remote ACCHSs compared with the urban site (Table 1). In adjusted models, the relative odds of PIMs were greater for females, those with kidney disease, urinary incontinence, depression, current heavy alcohol use and concerns for cognition (Table 2). Table 3 shows the most frequently used PIMs were psychotropics, including benzodiazepines (BZDs) (6.2%), tricyclic antidepressants (TCAs) and paroxetine or sedating antidepressants (4.5%).

Anticholinergic medications (ACB score ≥ 1) were prescribed for over a third of patients (38.3%; 95% CI = 33.8–43.1%), with 30.2% being prescribed these on a regular basis (regular medication-specific data not shown) (Table 1). Just over one in 10 patients (11.9%; 95% CI = 9.1–15.4%) had an ACB score ≥ 3, with 8.6% being prescribed such medications on a regular basis. ACB ≥1 prevalence was 51.4%, 28.4% and 34.7% at the urban, rural and remote ACCHSs respectively (Table 1).

Table 3 Potentially inappropriate medications criteria, with number and proportion detected in patients

Potentially inappropriate medications criteria	*n* (%)
PIMs relevant in most circumstances	
Any benzodiazepine	**28 (6.2)**
Antidepressants with high anticholinergic and sedative properties (tricyclic antidepressants and paroxetine)	**19 (4.5)**
Any metoclopramide	6 (1.4)
Anticholinergic medications with safer alternatives (excl. ophthalmic preparations)	6 (1.4)
Regular antipsychotics without a mental health indication	5 (1.2)
Long-term non-COX selective NSAIDs without gastric protection	2 (0.5)
Any long-acting sulfonylureas	2 (0.5)
Any Z-drugs (zolpidem and zopiclone)	2 (0.5)
Any indomethacin or ketorolac	1 (0.2)
Any nifedipine	1 (0.2)
Any central alpha-1 blockers	0 (0)
Any barbiturates	0 (0)
Any pethidine	0 (0)
Long-term nitrofurantoin	0 (0)
Any disopyramide	0 (0)
Any skeletal muscle relaxants	0 (0)
Drug–disease interactions	
Any with heart failure: cilostazol, non-dihydropyridine calcium channel blockers (diltiazem, verapamil), NSAIDs and thiazolidinediones (pioglitazone)	3 (0.7)
Any with incontinence in females: estrogens, peripheral alpha-1 blockers	3 (0.7)
Any history of delirium: anticholinergics, antipsychotics, benzodiazepines, corticosteroids (oral or parenteral), H_2 receptor antagonists and Z-drugs	2 (0.5)
Any with history of cognitive impairment: anticholinergics, benzodiazepines, antipsychotics and Z-drugs	3 (0.7)
Any with gastric or duodenal ulcers: NSAIDs without gastric protection	0 (0)
Drug–drug interactions	
Three or more CNS active agents	**18 (4.3)**
Any opioids and benzodiazepines	**8 (1.9)**
Any opioids and gabapentinoids	8 (1.9)
Any corticosteroids (oral or parenteral) and NSAIDs	6 (1.4)
Two or more of ACE inhibitors, ARBs or potassium sparing diuretics with kidney disease	4 (1.0)
Two or more anticholinergics	1 (0.2)
Any warfarin and amiodarone	1 (0.2)
Any warfarin and NSAIDs	1 (0.2)
Any warfarin and trimethoprim-sulfamethoxazole	1 (0.2)
Any lithium and ACE inhibitors	0 (0)
Any lithium and loop diuretics	0 (0)
Any phenytoin and trimethoprim sulfamethoxazole	0 (0)
Any theophylline and cimetidine	0 (0)
Any theophylline and ciprofloxacin	0 (0)
Any warfarin and ciprofloxacin	0 (0)
Any warfarin and macrolides (not azithromycin)	0 (0)

ACE, angiotensinogen-converting enzyme; CNS, central nervous system; COX, cyclooxygenase; NSAID, non-steroidal anti-inflammatory drug.
Bold = most frequently detected PIMs criteria.

Table 4 Univariable and multivariable regression analysis of factors associated with ACB score ≥1 or ≥3

	ACB score ≥ 1				ACB score ≥ 3			
	Univariable		Multivariable†		Univariable		Multivariable†	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age (years)	1.03 (1.00–1.05)	**0.035**	1.00 (0.97–1.03)	0.945	1.03 (0.99–1.06)	0.104	1.03 (0.99–1.07)	0.141
Female sex	1.39 (0.94–2.07)	0.102	‡		1.24 (0.68–2.25)	0.482	‡	
Health service								
Urban	1	**<0.001**	1	**<0.001**	1	**0.001**	1	**0.001**
Rural	0.37 (0.23–0.62)		0.31 (0.18–0.54)		0.09 (0.03–0.31)		0.10 (0.03–0.34)	
Remote	0.50 (0.31–0.81)		0.34 (0.19–0.60)		0.62 (0.33–1.17)		0.51 (0.25–1.04)	
Medical conditions								
Heart disease	2.65 (1.50–3.42)	**<0.001**	2.29 (1.39–3.80)	**0.001**	1.85 (1.02–3.36)	**0.042**	NS	
Atrial fibrillation	5.13 (1.63–16.21)	**0.005**	4.16 (1.18–14.66)	**0.026**	1.75 (0.48–6.38)	0.394	‡	
Hypertension	1.84 (1.23–2.74)	**0.003**	1.71 (1.06–2.76)	**0.027**	1.52 (0.83–2.77)	0.175	‡	
Diabetes	1.39 (0.92–2.08)	0.115	‡		1.05 (0.57–1.94)	0.864	‡	
Kidney disease	2.33 (1.46–3.71)	**<0.001**	1.93 (1.08–3.43)	**0.026**	2.95 (1.59–5.46)	**0.001**	3.07 (1.50–6.30)	**0.002**
Stroke	2.31 (1.14–4.65)	**0.019**	NS		2.42 (1.03–5.67)	**0.040**	NS	
Urinary incontinence	2.30 (0.91–5.85)	**0.080**	NS		2.83 (0.97–8.21)	0.056	‡	
Previous head injury	2.76 (1.12–6.80)	**0.028**	NS		1.81 (0.58–5.60)	0.306	‡	
History of depression	2.25 (1.50–3.38)	**<0.001**	2.13 (1.34–3.37)	**0.001**	3.08 (1.68–5.68)	**<0.001**	3.32 (1.70–6.47)	**<0.001**
Current smoker	1.27 (0.85–1.88)	0.238	‡		1.40 (0.77–2.53)	0.270	‡	
Current heavy alcohol use	1.33 (0.80–2.21)	0.266	‡		1.35 (0.66–2.77)	0.416	‡	
Concerns about cognition§	2.93 (1.57–5.45)	**0.001**	3.02 (1.51–6.03)	**0.002**	2.45 (1.16–5.20)	**0.019**	NS	
Identified cognitive impairment	1.36 (0.48–3.82)	0.562	‡		NA		‡	

†This column includes ORs only for age and other variables with statistically significant associations in a final multivariable model. Other variables with significant associations in univariable analysis did not reach statistical significance in the initial multivariable modelling and were excluded from the final multivariable model.

‡Variable not considered in multivariable modelling as it did not reach statistical significance in univariable analysis.

§Concerns about memory or thinking problems.

ACB, anticholinergic burden; CI, confidence interval; NS, not significant; OR, odds ratio.

Bold = statistically significant result ($P < 0.05$). NA = not applicable, insufficient data for analysis.

Table 5 Level 1 to Level 3 anticholinergic medications detected in patients

Anticholinergic medications	Total *n* (%)	Regular prescription *n* (%)	As needed prescription *n* (%)
Level 1			
Furosemide	32 (7.6)	30 (7.1)	2 (0.5)
Prednisolone	22 (5.2)	3 (0.7)	19 (4.5)
Codeine	22 (5.0)	2 (0.5)	20 (4.5)
Tramadol	20 (4.8)	7 (1.7)	13 (3.1)
Atenolol	18 (4.3)	18 (4.3)	0 (0)
Metoprolol	18 (4.3)	18 (4.3)	0 (0)
Sertraline	13 (3.1)	13 (3.1)	0 (0)
Diazepam	12 (2.9)	1 (0.2)	11 (2.7)
Oxycodone	11 (2.6)	6 (1.4)	5 (1.2)
Temazepam	9 (2.1)	2 (0.5)	7 (1.6)
Venlafaxine	8 (1.9)	8 (1.9)	0 (0)
Loperamide	5 (1.2)	0 (0)	5 (1.2)
Colchicine	4 (1.0)	1 (0.2)	3 (0.8)
Dipyridamole	4 (1.0)	4 (1.0)	0 (0)
Isosorbide mononitrate	4 (1.0)	4 (1.0)	0 (0)
Prochlorperazine	4 (1.0)	0 (0)	4 (1.0)
Morphine	3 (0.7)	1 (0.2)	2 (0.5)
Warfarin	3 (0.7)	3 (0.7)	0 (0)
Clonazepam	1 (0.2)	1 (0.2)	0 (0)
Digoxin	1 (0.2)	1 (0.2)	0 (0)
Fluoxetine	2 (0.5)	2 (0.5)	0 (0)
Fluvoxamine	2 (0.5)	2 (0.5)	0 (0)
Isosorbide dinitrate	2 (0.5)	1 (0.2)	1 (0.2)
Methadone	2 (0.5)	2 (0.5)	0 (0)
Risperidone	2 (0.5)	2 (0.5)	0 (0)
Alprazolam	1 (0.2)	1 (0.2)	0 (0)
Domperidone	1 (0.2)	0 (0)	1 (0.2)
Dosulepin	1 (0.2)	1 (0.2)	0 (0)
Haloperidol	1 (0.2)	1 (0.2)	0 (0)
Nifedipine	1 (0.2)	1 (0.2)	0 (0)
Olanzapine	1 (0.2)	1 (0.2)	0 (0)
Level 2			
Carbamazepine	2 (0.5)	2 (0.5)	0 (0)
Ranitidine	2 (0.5)	2 (0.5)	0 (0)
Hyoscine hydrobromide (scopolamine)	1 (0.2)	1 (0.2)	0 (0)
Nortriptyline	1 (0.2)	1 (0.2)	0 (0)
Level 3			
Amitriptyline	13 (3.1)	13 (3.1)	0 (0)
Paroxetine	4 (1.0)	4 (1.0)	0 (0)
Quetiapine	4 (1.0)	4 (1.0)	0 (0)
Tapentadol	4 (1.0)	4 (1.0)	0 (0)
Dexchlorpheniramine	3 (0.7)	1 (0.2)	2 (0.5)
Glycopyrronium	3 (0.7)	3 (0.7)	0 (0)
Aclidinium	1 (0.2)	1 (0.2)	0 (0)
Benzatropine	1 (0.2)	0 (0)	1 (0.2)
Chlorpromazine	1 (0.2)	1 (0.2)	0 (0)
Doxepin	1 (0.2)	1 (0.2)	0 (0)
Doxylamine	1 (0.2)	0 (0)	1 (0.2)
Oxybutynin	1 (0.2)	1 (0.2)	0 (0)
Promethazine	1 (0.2)	0 (0)	1 (0.2)

A small number of participants ($n = 5$) were taking a total of five over-the-counter and/or complementary medicine products that could not be classified.

In adjusted models, the relative odds of having ACB score ≥ 1 were lower in rural and remote ACCHSs compared to urban (Table 4). Chronic conditions remained significantly associated with higher odds of ACB score ≥ 1 after adjustment, and age was not significant. In adjusted models, significant ACB (ACB score ≥ 3) was associated with kidney disease, depression and attending an urban ACCHS (Table 4).

Levels 1–3 anticholinergic medications detected in this study are listed in Table 5, where frequencies for regular and as needed anticholinergic medications are reported separately. The most frequently prescribed anticholinergic medications were amitriptyline (3.1%), cardiac medications: furosemide (7.6%), atenolol (4.3%) and metoprolol (4.3%) and antidepressants: sertraline (3.1%) and venlafaxine (1.9%). The most common anticholinergic medications prescribed as needed were codeine (4.5%), tramadol (3.1%) and oxycodone (1.2%) and anxiolytics: diazepam (2.7%) and temazepam (1.6%), and prednisolone (4.5%) and loperamide (1.2%).

Figure S1 illustrates the frequency of patients with one or more medications, polypharmacy, PIMs and/or anticholinergic medications occurring concurrently. Of those prescribed one or more medications, 56 (19.0%) had combined polypharmacy, PIMS and anticholinergic medications. Of those with polypharmacy, 129 (70.9%) had PIMs or anticholinergic medications concurrently.

Discussion

This study provides important insight into the appropriateness of medication prescribing for older Aboriginal and Torres Strait Islander peoples. Across three ACCHSs, 43% of patients experienced polypharmacy. Other measures of potentially suboptimal prescribing were common; almost one in five had PIMs, and over one third were prescribed anticholinergic medications.

Overall, polypharmacy prevalence in this study was higher than that in the general older (70+ years) Australian population, 36% in 2017.[9] This is consistent with high levels of multimorbidity, including cardiovascular disease and diabetes occurring at younger ages where multiple regular medications are recommended.[2,25] Our findings concur with previous studies reporting PIMs for 20% of Aboriginal and Torres Strait Islander people in remote communities and regular anticholinergic medications among 47% of urban/regional Aboriginal communities. Significant ACB (score ≥ 3) was found in 12% in these

communities and 14% in the general older Australian population.[10,11,26]

Polypharmacy and potentially inappropriate prescribing frequently accompanied one another in this study. Of those with polypharmacy, 71% had concurrent PIMs or anticholinergic medications. In many cases, polypharmacy in the context of multimorbidity may be appropriate to prevent cerebrovascular disease and other chronic conditions.[27] However, the results of this study suggest that problematic polypharmacy is relatively prevalent in this population and could be a target for future interventions to improve prescribing and health outcomes. This is all the more compelling considering that PIMs dependent on diagnostic criteria were excluded in this study, indicating that rates are potentially higher than reported.

In this study, those with PIMs and anticholinergic medications were more likely to have concerns about their memory or thinking. Multiple conditions cause problems with memory and thinking, including dementia, depression, delirium and medication side effects, among others. For those with concerns about memory and thinking, medication review and rational deprescribing of PIMs and anticholinergic medications are important to reduce the potential effects of medication on cognition, and an area for further research.[28] Larger studies have reported a positive association between PIMs or ACB and cognitive impairment.[16,29,30]

Our results confirm previous research reporting a strong association between ACB and depression among Aboriginal and Torres Strait Islander peoples and in the general population.[11,16] Frequently detected anticholinergics in this study included amitriptyline, suggesting that tricyclic antidepressants may contribute to ACB for some older Aboriginal and Torres Strait Islander people.[11] Depressive symptoms also remain highest among those treated, suggesting a need for more culturally safe psychological services such as healing services for Elders. First-line therapy for depression involves non-pharmacological intervention, often accompanied by antidepressants prescribed over a limited time frame.[31] Prescription of antidepressants over longer periods is relatively common in Australian general practice, which may highlight an opportunity for re-evaluation of treatment or deprescribing of antidepressants for some.[32] Tricyclic antidepressants are more widely used among older groups compared to younger,[33] and this may be because of long-term use over many years and, potentially, reluctance to change to newer antidepressant agents as these become available. Prescription of tricyclic antidepressants, particularly at low dose, may also reflect off-label use such as for chronic pain, insomnia or urinary problems.[34]

Other frequently detected PIMs involve the prescription of benzodiazepines, sometimes concurrently with opioid agents. In Australia, prescriptions of benzodiazepines appear to be decreasing, likely because of emerging evidence surrounding associated cognitive impairment, falls and dependence.[35–37] However, high use of benzodiazepines, particularly among older and Aboriginal and Torres Strait Islander groups, suggests there is still some way to go to optimise prescribing for these groups.[38,39] In this study, benzodiazepines were prescribed for 6% of older patients in ACCHSs, some of which may be prescribed inappropriately. Improving access to culturally appropriate psychological services and educational interventions to optimise prescribing of anticholinergic antidepressants and benzodiazepines[38] are likely to benefit older ACCHS patients.

Health system factors may account for observed differences between ACCHSs in this study. Availability of on-site specialist services, screening programs and documentation practices at individual ACCHSs differ, and these factors likely affect documentation of chronic conditions. Such factors may account for the high remote ACCHS polypharmacy prevalence (55%), which was similar to that found in our previous study of older Aboriginal people in remote Kimberley communities who access several different mainstream and Aboriginal health services (53%).[10] Further, public funding for most medications dispensed at remote ACCHSs (under Section 100, National Health Act 1953) differs from arrangements at urban and rural ACCHSs (under Closing the Gap co-payment program); however, it is not clear whether this has influence over prescription practices in ACCHSs.[40,41]

Further research is required to understand differences with respect to health service and patient-related factors regarding suboptimal prescribing across urban, rural and remote areas and to understand adverse medication outcomes attributed to suboptimal prescribing. Trials of primary care interventions to address prescribing quality, such as on-site pharmacist review and culturally appropriate education for healthcare staff, may be beneficial.[42]

As a result of its cross-sectional nature, this study cannot draw conclusions about causal relationships. There may also be a bias towards people with more medical comorbidity in this study, owing to the exclusion of patients who had attended their health service less than three times over a 2-year period. Confounding because of medication indication or other factors may have influenced associations detected. Clinical information about specific medication indication, disease severity and geriatric syndromes could not be captured. Exact duration of medication therapy could not be determined, potentially leading to overestimation of potentially

suboptimal prescribing. On the other hand, there were likely patients with undocumented cognitive impairment in the sample, which may have led to an underestimation of potentially suboptimal prescribing. Medications prescribed elsewhere (at another primary care service, specialist doctor or hospital), over-the-counter and traditional medicines were not accounted for, which could also have led to an underestimation of polypharmacy, PIM use and ACB. Potentially inappropriate omission of medications based on relevant clinical information was not reported, though this often contributes to suboptimal prescribing.[6,10] Additionally, this is a study of prescribed medication rather than 'as taken' medication and concordance may be suboptimal.

For some patients, instances of potentially suboptimal prescribing identified may be appropriate. This study could not account for various medication-related factors that influence prescribing practices, such as patient preference or clinical judgement. PIM criteria and the ACB scale applied in this study were developed and validated for adults aged ≥65 years,[12,21] whereas this study included people aged ≥50 years. Although Aboriginal and Torres Strait Islander people aged ≥50 years are frequently considered to be of older age, these tools have not been validated in this younger population, and use may not be appropriate for all individuals. Although we tried to control for relevant factors in our regression models, some residual confounding may remain. This study and prevalence of potentially suboptimal prescribing should be interpreted with caution and with consideration of a patient's individual clinical circumstances and personal preferences regarding their healthcare.

A key strength of this study is that prescription medications and cognitive impairment risk factors were recorded directly from electronic patient records, which were maintained by practice staff, including GPs, nurses and Aboriginal Health Practitioners. Both regular and as-needed medications were captured to comprehensively determine PIMs and ACB, although inclusion of the latter might lead to an overestimation of potentially suboptimal prescribing. PIMs and ACBs were measured with reference to widely utilised literature, and, where relevant, measures were adapted to reflect local availability of medications.[12,21–24] The sample size allowed for the assessment of important characteristics associated with potentially suboptimal prescribing.

Conclusion

In summary, polypharmacy affected almost half of older patients at urban, rural and remote ACCHSs in this study. Prevalence of PIMs and anticholinergic medications among patients was similar to estimates reported for Aboriginal and Torres Strait Islander communities elsewhere in Australia. Strong associations between polypharmacy, PIMs, ACBs and cognitive risk factors such as depression suggest patients with these conditions would benefit from regular medication review with the objective of minimising medication-related harm. The annual health check for Aboriginal and Torres Strait Islander people is an opportunity to review medications for all older people. Interventions to optimise prescribing practices in ACCHSs should also target those with risk factors for cognitive impairment and those expressing concerns about their memory or thinking.

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Data Availability Statement

Research data are not shared.

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Supporting Information

Additional supporting information may be found in the online version of this article at the publisher's web-site:

Figure S1. Venn diagram of patients taking at least one medication.
Table S1. Medications included in the anticholinergic cognitive burden scale.