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Potentially suboptimal prescribing of medicines for older Aboriginal Australians in remote areas

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Potentially suboptimal prescribing of medicines for older Aboriginal Australians in remote areas

Abstract

Objectives: To investigate the prevalence of polypharmacy, under-prescribing and potentially inappropriate medicine use among Aboriginal Australians living in remote Western Australia.

Design: Cross-sectional study.

Setting: Six remote communities in the Kimberley and the town of Derby, Western Australia.

Participants: Aboriginal people aged 45 years or more with complete medication histories.

Main outcome measures: Proportions of patients with medicine histories indicating polypharmacy, potential under-prescribing of indicated medicines, or potentially inappropriate prescribing (including potential prescribing cascades or drug interactions).

Results: Complete medicine histories were available for 273 participants. The mean number of prescribed medicines was 5.1 (SD, 3.6). At least one form of suboptimal prescribing was identified for 166 participants (61%), including polypharmacy for 145 (53%), potential under-prescribing of at least one indicated medicine for 33 (12%), and potentially inappropriate prescribing for 54 participants (20%). Potential prescribing cascades or drug interactions were identified for 12 participants (4%).

Conclusions: Potentially suboptimal prescribing affected more than half the participating older Aboriginal Australians from the Kimberley. If generalisable to other remote Indigenous Australians, the prevalence of polypharmacy, potentially inappropriate prescribing, and under-prescribing of indicated medicines is problematic, and suggests that older Indigenous people in remote areas are at risk of medicine-related harm.

Summary box

The known: Suboptimal prescribing for older people is generally associated with poor health outcomes. Rates of chronic disease and comorbidity for older Aboriginal Australians are high.

The new: We evaluated polypharmacy (five or more concomitantly prescribed medicines), under-prescribing of indicated medicines, and inappropriate prescribing for older Aboriginal people in the remote Kimberley. Suboptimal prescribing was identified for 53% of the

participants. Under-prescribing of indicated medicines was less frequent than other suboptimal prescribing.

The implications: Culturally appropriate, targeted strategies are required for improving prescribing for older people in remote Aboriginal communities.

It is forecast that the number of Aboriginal and Torres Strait Islander (Indigenous) Australians aged 65 or more will double between 2011 and 2026.¹ Older Indigenous people frequently have several chronic conditions, including diabetes mellitus and cardiac disease,² particularly those living in remote areas, where chronic conditions and frailty develop at younger ages than in Indigenous Australians elsewhere.^{3,4} Effectively managing the medications for these conditions and symptoms is critical for reducing the risk of acute adverse events, functional decline, and premature mortality.

The general risk and consequences of suboptimal prescribing of medications for older people has been investigated. For example, not prescribing an indicated medicine means that its potentially beneficial clinical effects cannot be realised.⁵ Polypharmacy — the concurrent use of five or more prescribed medicines — is associated with poor clinical outcomes such as falls, frailty, and hospitalisation.⁶ Polypharmacy can be appropriate if clinical circumstances and personal care goals indicate that the medicines are all indicated, but it is often inappropriate in older and potentially frail people.⁵

In addition to the usual challenges of optimising medical regimens for older people, older Indigenous people experience additional barriers to appropriate health care, including reduced accessibility, dispossession, racism, and economic disadvantage.⁷ Research into medicine use by Indigenous Australians has focused on accessibility and service delivery, adherence, and management. Although poor adherence to prescribed medications by Indigenous people has been reported,⁸ a recent systematic review found that adherence rates were not markedly lower than for other Australians.⁹ Information on the quality of prescribing for older Indigenous people in remote Australia is limited; expenditure on medicines for Indigenous Australians has been historically lower than for other Australians, but it is unclear whether polypharmacy is a particular problem.¹⁰

It remains unclear whether suboptimal prescribing, including polypharmacy and under-prescribing, for older Indigenous Australians living in remote areas is similar to that for other Australians.¹⁰ We therefore evaluated the prevalence of polypharmacy, under-prescribing, and potentially inappropriate prescribing for Aboriginal people in the Kimberley region aged 45 years or more. This investigation was a subproject of the Kimberley Healthy Adults Project.^{3,11-13}

Methods

Study design and setting

We undertook a cross-sectional study of older Aboriginal Australians living in remote Western Australia. The Kimberley is a remote region of northern Western Australia

covering 421 451 km² (population: about 36 000). Almost half the population (47%) are Aboriginal Australians from five major language family groups, 65% of whom live in very remote areas. There are more than 200 communities and outstations in the Kimberley, but only three towns with populations greater than 2000; 15 communities include at least 30 people aged 45 years or more.¹⁴

As a comprehensive sampling frame for the Kimberley was not available because the Aboriginal population are under-represented on the electoral roll, and it would have not been feasible to complete a comprehensive survey of the region,¹⁵ we applied semi-purposeful sampling to select the communities from which we recruited participants. We developed a representative sample of the region in consultation with the Kimberley Language Resource Centre (Halls Creek); in accordance with their recommendation, we stratified the communities by language family to ensure that the selected communities reflected the diverse region and its population.¹⁵ From a sampling frame of the five Kimberley language families that included the 15 remote communities with at least 30 people aged 45 years or more, we randomly selected five Aboriginal communities (Wirrimanu, Mowanjum, Warmun, Junjuwa, and Looma). An additional community, Ardyaloon, was purposively selected to include a saltwater community, as was one town (Derby; Aboriginal proportion of population, 49%¹⁶).

Participants

Community approval was gained before commencing recruitment. Aboriginal Australians living in the Kimberley aged 45 years or more were recruited during Feb 2011 – June 2013 in the second wave of the Kimberley Healthy Adults Project (commenced 2002); 5.7% of people approached declined to take part. The age threshold was based on the Australian government definition of older age for Aboriginal Australians, given their lower life expectancy and greater disease burden than for other Australians. The sample represented 17% of Aboriginal people aged 45 years or more living in the Kimberley.¹³

All Aboriginal Australians aged 45 years or more who lived in the six selected remote communities were invited to participate in the study. Local health services provided lists of community members of appropriate age, and these were updated by local Indigenous community workers. We also invited one-third of the Aboriginal people living in Derby aged 45 years or more, based upon an amalgamated list of people who had attended Derby Health Services and the Derby Aboriginal Health Service. Community leaders, aged care workers, and research assistants facilitated identifying Aboriginal people aged 45 years or more in the included communities. We excluded participants with incomplete medication histories (ie, those without data in the MMEx and Communicare electronic patient record systems. Further details of our methodology have been published elsewhere.¹¹

Data collection

We individually extracted data on the prescribed medicines and diagnoses of consenting participants from their electronic medical records, routinely used by all primary care

services in the Kimberley for Pharmaceutical Benefits Scheme (PBS) prescribing and for dispensing medications under the PBS section 100 exemption for remote area Aboriginal health services. The electronic medical record system (MMEx), introduced because of the problems associated with a mobile population in a large remote geographic region, can be accessed (with patient consent) by all health care providers in the Kimberley, including specialists, hospitals, aged care providers, and allied health professionals. MMEx was developed as a collaboration between the Kimberley Aboriginal Medical Service and the University of Western Australia to provide a centralised online electronic medical record system. MMEx has been the sole medical record system for all Aboriginal Community Controlled Health Services (ACCHS) clinics across the Kimberley for more than ten years, and also for five major WA Country Health Services remote clinics, including those in Warmun, Looma and Ardyaloon.

Patients from five of the six selected remote communities and from Derby had MMEx records. Participants in Derby and from the nearby community of Mowanjum generally used primary health care services at the Derby Aboriginal Health Service (an ACCHS), the only comprehensive primary health care service in Derby. People in Junjuwa usually visited Fitzroy Crossing for health care, where the Communicare medical record system is used. Data on the accuracy and completeness of MMEx are not available; demographic data and data on chronic conditions for Kimberley people with Communicare records are 98–100% accurate and complete, but can be incomplete for acute conditions.¹⁷

Medicines were coded according to the *Anatomical, therapeutic, chemical classification* of the World Health Organization (ATC/DDD system).¹⁸

In semi-structured interviews, we ascertained the self-reported age of each participant, their sex, preferred language, self-reported medical history, and whether they had received any formal education. We assessed cognition and depression with the Kimberley Indigenous Cognitive Assessment cognitive (KICA-Cog)¹⁹ and depression scales (KICA-Dep);²⁰ depression was defined as a KICA-Dep score of at least 8, cognitive impairment as a KICA-Cog score of 35 or less. During the interview, we asked participants about their smoking and alcohol consumption (“Do you smoke? Do you chew tobacco? Do you drink grog?”; each with “yes” or “no” responses). We measured each participant’s height (to 0.1 cm) and weight (to 0.1 kg) and calculated their body mass index (BMI; very underweight, < 18 kg/m²; underweight, 18–19.9 kg/m²; normal, 20–24.9 kg/m²; overweight, 25–29.9 kg/m²; obese, ≥ 30 kg/m²). For assessing under-prescribing, we analysed diagnosis data from their electronic medical record, cross-referenced with medicines data from the same source.

Markers of potentially suboptimal medicine prescribing

Published criteria for assessing prescribing quality, particularly those relevant to Australia,^{21–24} were used to compile a list of potentially inappropriately prescribed medicines and to define markers of suboptimal prescribing, including potential under-prescribing (Box 1). Medicines included in the Beers criteria, a consensus list of medicines with a higher risk of harm for older people,²¹ were defined as potentially

inappropriate medicines. As dosage data were not available, we included some medicines (such as ferrous sulphate, included in the Beers criteria for daily doses exceeding 325 mg) as “additional medicines that pose a potential increased risk of harm”. We defined under-prescribing according to an Australian list based on local data.²²

Simultaneously holding prescriptions for five or more medicines was defined as polypharmacy, consistent with empiric evidence that five medicines is the threshold at which the risk of medicine-related harm for older people is increased.⁶

Statistical analyses

Data were analysed in Stata 11.2 (StataCorp). We summarised the data as descriptive statistics (means with standard deviations [SDs], proportions) and compared the distribution of categorical variables in Pearson χ^2 tests. We explored factors associated with the outcomes of interest in binary logistic regressions, testing model goodness-of-fit in Hosmer–Lemeshow tests. All variables significant in univariate analyses were included in the multivariable model, after which non-significant covariates were removed in a manual, backwards manner. $P < 0.05$ was deemed statistically significant.

Ethics approval

We obtained approval for this study from the relevant community councils, the Kimberley Aboriginal Medical Service, and the Kimberley Aboriginal Health Planning Forum Research Subcommittee (reference, 2010-002). Approval was also provided by the human research ethics committees of the University of Western Australia (reference, RA/4/1/4065) and the WA Department of Health (reference, 2013/26), and by the Western Australian Aboriginal Health Ethics Committee (reference, 281 04/10). All participants provided written informed consent.

Results

A total of 387 Aboriginal people were invited to participate; as 98 people could not attend for various reasons, 289 (75%) were recruited for the study (228 from the six settlements, 61 from Derby). Complete medicine records were available for 273 (94%) of the recruited participants (220 from the six settlements, 53 from Derby); the demographic, lifestyle, and health characteristics of the full sample and those included in our analysis were similar (Box 2). The mean age of the 273 participants with complete medication histories was 61.2 years (SD, 11.1 years); 150 were women (55%). Participants were prescribed a mean 5.1 medicines (SD, 3.6; range, 0–16). Suboptimal prescribing was identified for 166 participants (61%), including 55 people (20%) with more than one potential problem (Box 3).

Polypharmacy and potential under-prescribing

Polypharmacy was identified for 145 participants (53%) (Box 3, Box 4); the proportion increased with age, but not to a statistically significant degree (Box 5). Diabetes, heart

problems, and higher BMI were significantly associated with polypharmacy, while having some formal education was protective (Box 6).

Potential under-prescribing of indicated medicines was identified for 33 participants (12%), including 17 of 27 participants (63%) with a history of coronary heart disease and 5 of 12 participants (42%) with a history of stroke. Under-prescribing was less frequent for participants with a history of atrial fibrillation (3 of 16, 19%) or a history of hypertension (10 of 139, 7%). There were no systematic associations of under-prescribing with age, sex, or education (Box 5).

Potentially inappropriate prescribing

Fifty-four participants (20%) had been prescribed at least one potentially inappropriate medicine (at least one medicine relatively contraindicated or with increased risk of harm in older people, or a prescribing cascade). There were no systematic associations of potentially inappropriate prescribing with age, sex, or education (Box 5). We found a positive association between potentially inappropriate prescribing and each of diabetes and stroke, and a negative association with chewing tobacco (Box 6).

Thirty-four participants (12%) had been prescribed one or more medicines relatively contraindicated in older people; 31 (11%) had been prescribed one relatively contraindicated medicine, three (1%) had been prescribed two. Medicines that pose an increased risk of harm in older people were prescribed for 23 participants (8%). Single potential prescribing cascades or drug interactions were identified for 12 participants (4%); for example, eight participants (3%) who reported drugs for obstructive airway diseases were also prescribed β -adrenoceptor blockers.

Discussion

Three of five older Aboriginal Australians in our study had at least one problem of potentially suboptimal prescribing, including polypharmacy for 53% of participants and potential under-prescribing of indicated medicines for 12%. Potentially inappropriate prescribing and prescribing cascades affected one in five participants.

Our findings suggest that polypharmacy affects remote Aboriginal people at a younger age than other Australians. Although not directly comparable with our sample, it has been reported that polypharmacy affected 36% of people in Perth aged 70 years or more,²⁵ with similar rates for community-dwelling people in Sydney over 65.²⁶ Our finding that polypharmacy is common among remote Aboriginal people contrasts with historically lower medicine expenditure for Indigenous Australians.¹⁰ However, a high prevalence of polypharmacy might be expected given the higher rates and numbers of chronic diseases at younger ages in Aboriginal people, consistent with the generally greater prevalence of polypharmacy among people with diabetes, heart disease, or overweight.⁴ Polypharmacy may therefore be appropriate, but it can also be harmful.⁶ While increasing the accessibility of medicines for Indigenous Australians is important, improving prescribing practices and optimising medicine use in remote populations may also be required.

We found that one in eight remote Aboriginal people were not prescribed one or more indicated medicines. While this finding is worrying, the proportion is substantially lower than the reported 57% for older men in a Perth community study.²⁵ The lower level we found is again surprising given the lower level of medicine expenditure for Aboriginal people.¹⁰

Seemingly suboptimal medicine prescribing may actually have been appropriate for some individuals. The preferences of patients may have influenced rates of potentially suboptimal prescribing, as would the clinical judgement of prescribers. However, it remains likely that suboptimal prescribing increases the risk of poor health outcomes for remote Aboriginal Australians, and interventions that optimise prescribing are needed.⁵ Simple interventions, such as prescriber alerts and education, could be trialled, but the complexity of prescribing practices in communities with limited medical access probably requires a combination of responses.

Limitations

Our study is the first to evaluate potentially inappropriate medicine prescribing for Aboriginal people in remote Australia. While the participation rate after approaching the entire populations of the six participating communities was good, semi-purposeful sampling of communities meant that our sample is not fully representative of the region; whether our results are generalisable to the entire Kimberley or to other remote Australian communities is therefore uncertain. Further, as we analysed cross-sectional data, causality cannot be inferred; diagnostic data in the electronic medical records may have been incomplete; and medicine doses were unavailable for analysis.

Data for prescribed medicines and diagnoses were both derived from the participants' electronic medical records, which both maintained consistency and assessed information that is also available to prescribers at the point of care. However, information about traditional medicines was not included in these records, and the medicines prescribed for participants may not have been the same as those they actually used. However, adherence to medicine regimens is similar for Indigenous people and other Australians,⁹ despite suggestions of lower adherence among Indigenous Australians.⁸ Finally, we could not consider the individual clinical circumstances of each participant, and it is likely that polypharmacy or under-prescribing was clinically appropriate in some cases.

Conclusion

Suboptimal prescribing, including polypharmacy, was common among older Aboriginal people in the Kimberley. Interventions, such as prescriber alerts and targeted training for remote area medical professionals in appropriate prescribing for older people, in conjunction with continuing to increase access to appropriate medicines, may improve prescribing in remote areas. It is likely, however, that multifaceted solutions will be required for this complex problem. Culturally appropriate interventional studies should assess strategies for reducing the prevalence of suboptimal prescribing in remote Aboriginal communities.

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Box 1. Markers of suboptimal medication prescribing

Variable	Definition
Polypharmacy	Five or more concomitantly prescribed medicines: this is the most common definition of polypharmacy, and is consistent with findings that five medications is the threshold for increased risk of medicine-related harm in older people.⁶
Potential under-prescribing	- History of atrial fibrillation, and antiplatelet agent or anticoagulant therapy not prescribed; OR - History of stroke, and angiotensin-converting enzyme (ACE) inhibitor/angiotensin II antagonist and statin not prescribed; OR - History of ischaemic heart disease, and antiplatelet agent, ACE inhibitor/angiotensin II antagonist, β-

blocker, and statin therapy not prescribed; OR

- History of hypertension, and antihypertensive, diuretic, β -blocker, calcium channel blocker, ACE inhibitor/angiotensin II receptor antagonist therapy not prescribed.

Potentially inappropriate
prescribing

- Prescribing of a medicine relatively contraindicated in older people (benzodiazepines, barbiturates, mianserin, tricyclic antidepressants, phenothiazines, non-steroidal anti-inflammatory drugs (NSAIDs), dextropropoxyphene, cyproheptadine, propantheline, amantadine, benzhexol/benzotropine, methyl dopa, cimetidine, sulfonamide–trimethoprim combinations, disopyramide, hydrochlorothiazide–potassium-sparing diuretic combinations, glibenclamide, theophylline, fluoxetine, antihistamines, oxybutynin, ergot alkaloids, nitrofurantoin, amiodarone, nifedipine, clonidine/apraclonidine, promethazine, dicyclomine, hyoscyamine, ticlopidine, dexamphetamine); OR
- Prescribing of a medicine with a higher risk of harm in older people (digoxin, ferrous sulphate, antipsychotics, allopurinol, prazosin, warfarin when combined with an NSAID); OR
- Prescribing of medicines suggesting either a prescribing cascade or a drug interaction (cholinesterase inhibitors with systemic anticholinergics, antiparkinsonians with dopamine antagonists, diuretics with NSAIDs, thiazides with anti-gout therapy, β -blockers with drugs for obstructive airway diseases).

Box 2. Demographic, lifestyle, and health characteristics of the recruited participants, by availability of complete medicine history

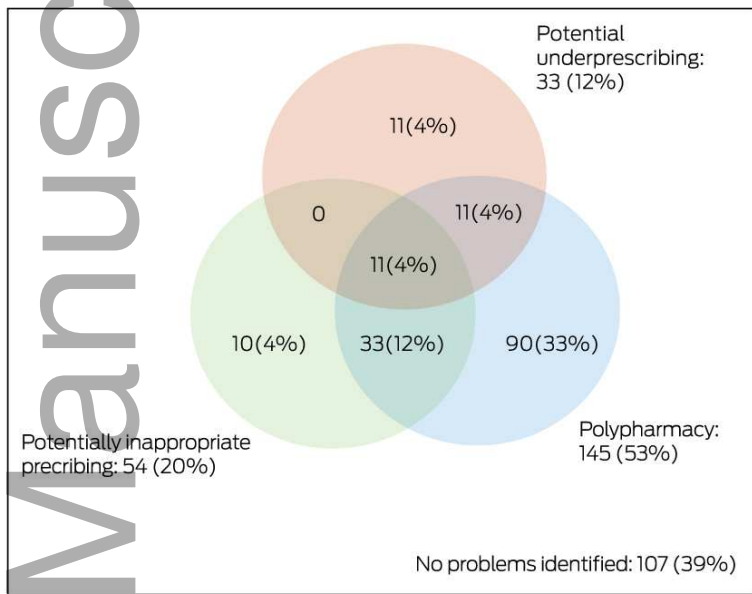
	All participants	Participants with complete medicines history*	Missing data (complete history group)
Total number of participants	289	273	
Sex			0
Men	128 (44%)	123 (45%)	
Women	161 (56%)	150 (55%)	
Age (years)			0
45–49	45 (16%)	42 (15%)	
50–59	111 (38%)	105 (38%)	
60–69	61 (21%)	58 (21%)	
70–79	47 (16%)	45 (16%)	
80 or more	25 (9%)	23 (8%)	
At least one year of formal education	217 (75%)	202 (74%)	5
Lifestyle			
Drinks alcohol	109 (38%)	102 (37%)	7
Smokes	96 (33%)	88 (32%)	7
Chews tobacco	87 (30%)	83 (30%)	8
Body mass index (kg/m ²)			49
Very underweight (< 18)	12 (4%)	11 (4%)	
Underweight (18–19.9)	14 (5%)	12 (4%)	
Normal (20–24.9)	61 (21%)	59 (22%)	
Overweight (25–29.9)	77 (27%)	73 (27%)	
Obese (≥ 30)	73 (25%)	69 (25%)	
Medical history and findings			
Impaired eyesight	129 (45%)	120 (44%)	5
Impaired hearing	52 (18%)	51 (19%)	8
Cognitive impairment (KICA-Cog ≤ 35) ¹⁹	62 (21%)	60 (22%)	43
Depression (KICA-Dep > 8) ²⁰	60 (21%)	56 (21%)	19
Stroke	37 (13%)	33 (12%)	6
Diabetes	131 (45%)	122 (45%)	5
Hypertension	111 (38%)	104 (38%)	8
Head injury	89 (31%)	86 (32%)	11
Poor mobility	118 (41%)	112 (41%)	9
Pain	154 (53%)	147 (54%)	11

Heart condition	72 (25%)	70 (26%)	6
Kidney condition	68 (24%)	65 (24%)	5
Urinary incontinence	71 (25%)	65 (24%)	12
Recent fall	61 (21%)	59 (22%)	11

KICA-Cog = Kimberley Indigenous Cognitive Assessment cognitive assessment; KICA-Dep = Kimberley Indigenous Cognitive Assessment depression scale.

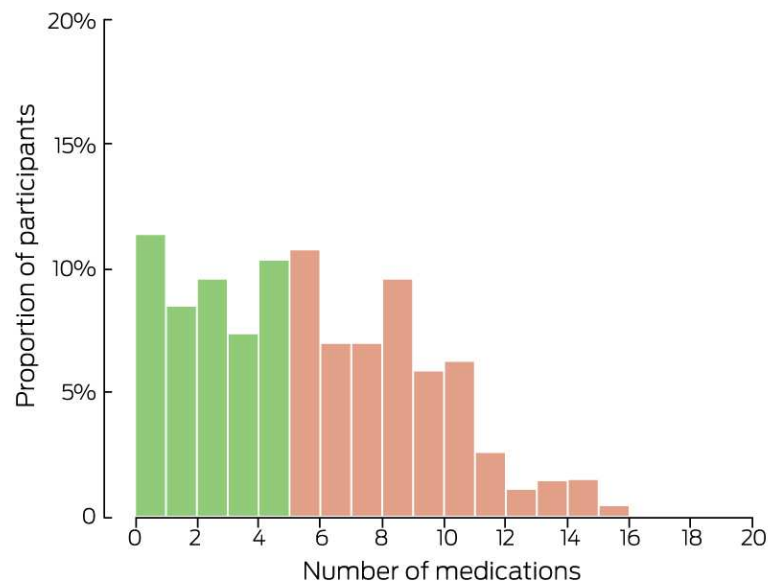
* Proportions calculated without excluding missing data.

Box 3. Suboptimal prescribing of medicines for 273 participants with complete



medicine records

Box 4. Distribution of the 273 participants according to the number of their prescribed medicines*



* Red bars: polypharmacy (five or more prescribed medicines).

Box 5. Suboptimal prescribing of medicines for the 273 participants, by sex, age, and education

	Polypharmacy		P	Under-prescribing		P	Inappropriate prescribing		P	Suboptimal prescribing: total		P
	No	Yes		No	Yes		No	Yes		No	Yes	
Participants	128 (47%)	145 (53%)		240 (88%)	33 (12%)		219 (80%)	54 (20%)		107 (39%)	166 (61%)	
Sex	0.94			0.06			0.42			0.96		
Men	58 (47%)	65 (53%)		103 (84%)	20 (16%)		96 (78%)	27 (22%)		48 (39%)	75 (61%)	
Women	70 (47%)	80 (53%)		137 (91%)	13 (9%)		123 (82%)	27 (18%)		59 (39%)	91 (61%)	
Age (years)	0.38			0.60			0.71			0.63		
45–49	22 (52%)	20 (48%)		37 (88%)	5 (12%)		34 (81%)	8 (19%)		20 (48%)	22 (52%)	
50–59	54 (51%)	51 (49%)		96 (91%)	9 (9%)		88 (84%)	17 (16%)		43 (41%)	62 (59%)	
60–69	27 (47%)	31 (53%)		48 (83%)	10 (17%)		44 (76%)	14 (24%)		21 (36%)	37 (64%)	
70–79	17 (38%)	28 (62%)		39 (87%)	6 (13%)		36 (80%)	9 (20%)		16 (36%)	29 (64%)	
80 or more	8 (35%)	15 (65%)		20 (87%)	3 (13%)		17 (74%)	6 (26%)		7 (30%)	16 (70%)	

At least one year of formal education	0.008		0.56		0.55		0.031	
Yes	103 (51%)	99 (49%)	180 (89%)	22 (11%)	159 (79%)	43 (21%)	84 (42%)	118 (58%)
No	21 (32%)	45 (68%)	56 (85%)	10 (15%)	56 (85%)	10 (15%)	19 (29%)	47 (71%)

Box 6. Factors associated with potentially suboptimal prescribing for 273 participants: logistic regression analyses

Variable	Polypharmacy (5 or more medicines)		Inappropriate prescribing	
	Univariate OR (95% CI)	Multivariable* OR (95% CI)	Univariate OR (95% CI)	Multivariable* OR (95% CI)
Age (per year)	1.03 (1.00–1.05)	—	1.01 (0.98–1.03)	
Sex (women)	1.02 (0.63–1.64)	—	0.78 (0.43–1.42)	
Some formal education	0.45 (0.25–0.81)	0.28 (0.11–0.72)	1.51 (0.71–3.21)	
Poor eyesight	0.86 (0.53–1.39)	—	0.73 (0.39–1.35)	
Poor hearing	1.05 (0.57–1.94)	—	1.00 (0.46–2.16)	
Stroke	2.64 (1.18–5.93)	—	2.62 (1.19–5.75)	2.19 (0.94–5.11)
Diabetes	12.2 (6.67–22.4)	15.9 (7.08–35.6)	2.53 (1.34–4.76)	2.61 (1.35–5.05)
Hypertension	3.88 (2.22–6.80)	NS	1.51 (0.79–2.89)	
Heart problems	4.47 (2.35–8.49)	6.20 (2.31–16.6)	1.50 (0.77–2.93)	
Kidney problems	2.17 (1.19–3.93)	NS	0.74 (0.35–1.55)	
Incontinence	1.64 (0.92–2.92)	—	1.03 (0.51–2.07)	
Poor mobility	1.85 (1.13–3.05)	NS	1.33 (0.72–2.45)	
Recent fall	1.81 (0.99–3.30)	—	1.20 (0.59–2.45)	
Pain	1.36 (0.83–2.22)	—	1.17 (0.63–2.17)	
Head injury	0.81 (0.48–1.36)	—	1.04 (0.54–1.99)	
Current drinker	0.57 (0.34–0.93)	NS	0.88 (0.47–1.64)	
Current smoker	0.53 (0.32–0.89)	NS	0.94 (0.50–1.80)	
Chews tobacco	1.26 (0.74–2.12)	—	0.44 (0.21–0.93)	0.39 (0.18–0.85)
Body mass index (per 1 kg/m ²)	1.08 (1.03–1.13)	1.08 (1.02–1.15)	1.01 (0.95–1.06)	
Depression ¹⁹	1.02 (0.97–1.06)	—	1.01 (0.95–1.07)	
Cognitive impairment ²⁰	1.00 (0.94–1.07)	—	1.03 (0.94–1.13)	

CI = confidence interval; NS = non-significant; OR = odds ratio. * This column includes ORs only for variables with significant associations in the final multivariable model; five other variables with significant associations in univariate models were not significant in the initial multivariable model, and were not included in the final model.