Evaluation of the Effect of an Intervention on Potentially Inappropriate Medications (PIMS), Polypharmacy and Anticholinergic Burden Scores for People with Dementia; Results from the SMS Dementia Study†: A Quasi-Experimental Study

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Abstract

Background People with dementia (PWD) are at risk for medication related harm due to their impaired cognition and frequently being prescribed many medications. Few previous studies of PWD inpatients have been focused on medication safety interventions.

This study aimed to evaluate an intervention designed to improve medication safety for people with dementia (PWD) and their carers during an unplanned admission to hospital. This article reports the effect of the intervention on potentially inappropriate medications (PIMs), polypharmacy and anticholinergic burden scores for PWD in the study.

Methods A quasi-experimental pre-post design using an intervention site and a control site was conducted in 2017-2019, in a regional area in New South Wales, Australia. PIMs, polypharmacy and anticholinergic burden were measured at admission, discharge and three months after discharge. In addition, medication reconciliation at admission and scoring of pharmacists recommendations using severity and relevance scores were measured.

Results There were 628 participants including 350 in the post-intervention phase. Polypharmacy for these admissions was high, and there was approximately 30% reduction in the number of medications at discharge. PIMs at admission were also high, and decreased significantly at discharge however there was no treatment effect associated with the intervention. The mean anticholinergic burden score also decreased significantly between admission and discharge, however, no treatment effect was seen.

Conclusions High rates of polypharmacy and PIMs in this study indicate this study population was admitted with multiple comorbidities. Reduced PIMs at discharge were correlated with reduced anticholinergic burden. Medication reconciliation resulted in many recommendations that contributed to the reductions in medications. Although the study did not report a treatment effect, reductions in the number of medications and PIMs reduced medication related risk for PWD.

Reduced risks associated with inappropriate or unnecessary medications can reduce hospital admissions and adverse events for PWD. This intervention was feasible to implement, and future multisite studies should be designed to recruit larger study samples to evaluate interventions for improving medication safety for PWD. They should also adopt routine screening for cognitive impairment to identify PWD at admission.

Background

People with dementia (PWD) have a high risk for adverse health outcomes associated with medications due to being cognitively impaired [1]. This manifests as missing medications due to confusion or memory problems, or taking incorrect medications or dosages. The risk increases for PWD who don't have a carer, have multiple comorbidities and consequently have more than five medications prescribed for them (polypharmacy) [2, 3], and who are prescribed potentially inappropriate medications (PIMs) [4]. PIMs are defined as "medications that pose potential risks that outweigh potential benefits" [5]. PIMs pose a risk for PWD because they may have side effects that exacerbate confusion and balance problems (resulting in falls) and increase anticholinergic burden. When PWD are admitted to hospital, they may also suffer escalated behavioural and psychological symptoms of dementia (BPSD) and may be temporarily managed with PIMs such as psychotropics, sedatives or hypnotics.

Antipsychotics have been identified as being overused and having limited clinical benefit for BPSD [6, 7] and should not be continued for more than three months [8]. Consequently, the risk for PWD remains high if these medications are not discontinued at discharge [9]. The prevalence of PIMs for PWD in the community has been reported in a systematic review, to range from 10–56% and is higher in nursing home settings [5]. However, the prevalence of PIMs in hospital has been reported in another systematic review to be 53–90% for inpatients with cognitive impairment [10]. These reviews provide evidence to confirm that PIMs are an important clinical issue that requires further attention. Two previous studies have compared PIMs between admission and discharge and reported that PIMs for PWD were significantly reduced at discharge (Mean 4.0 reduced to 3.3, difference 0.7, $p < 0.0001$) in a study of 277 admissions [1], and (Mean reduced from 0.8 to 0.4, difference 0.4, $p = 0.01$) in a study of 118 admissions [11]. When PWD are admitted to hospital, there is an opportunity to undertake medication reconciliation and to identify PIMs and other medications that may no longer be required. Where it is possible to reduce medications, the risk for PWD is also reduced. Some previous intervention studies have been conducted to reduce PIMs in community/primary care settings [12–14] and nursing homes, for older people [15]; however no studies have been conducted in hospital settings or on PWD for this purpose. Previous studies of older people in non-hospital settings used interventions such as education interventions, medication reviews and collaborative care approaches. Significant reductions in PIMs were reported from using medication reviews and an educational intervention. In addition, a prospective observational study of 991 pharmacist interventions for 557 patients during medication reconciliation in an emergency department, reported that medication errors were severe in 57% of cases, and that 65% of the interventions were relevant [16]. This suggests that pharmacist medication reconciliation can be used to reduce PIMs, and polypharmacy, as well as to reduce medication errors. An intervention study involving hospital pharmacists completing the medication management plan in the medical discharge summary also reported a significant reduction in the rate of medication errors at discharge [17]. Furthermore, a study that evaluated a collaborative care approach involving clinical pharmacist medication review, in which the clinical pharmacist was based in the community health centre with the general practitioner (GP); reported that 48% of recommendations were accepted by GPs in an elderly community population (n = 91) [13]. The results of these previous studies suggest that it is important to undertake research to evaluate the effectiveness of pharmacist interventions for PWD in the acute care setting to reduce PIMs (and associated anticholinergic burden), and polypharmacy and measure the frequency of medication prescribing errors for these vulnerable admitted patients.

Methods

This study aimed to evaluate an intervention designed to improve medication safety for PWD and their carers during an unplanned admission to hospital and the effect on the primary outcomes are reported separately. This article reports the effect of the intervention on PIMS, polypharmacy and anticholinergic burden scores for PWD in the study. In addition, we report the impact of the intervention on the frequency of medication reconciliation at admission and subsequent medication recommendations for PWD. A quasi-experimental pre-post design was used because participants could not be randomised at the study sites. The study was conducted at two regional hospitals in New South Wales, Australia, between October 2017 and September 2019. Usual care was delivered during phase one at both hospitals. In phase two, the intervention was delivered at the intervention hospital and the other hospital was used as a control site.

Participants were PWD or older people who had a positive screen for memory problems or confusion (excluding transient delirium), during an index admission via the emergency department (ED) during the study period. Proxy consent was provided by their carer or person responsible. Additional detail about participant eligibility is provided in a previous publication [1].

Data were collected using purpose-developed clinical audit instruments for admission (usually within 48 hours), and discharge (usually within 24 hours), and medications from medical records to measure PIMs, numbers of medications and to calculate the anticholinergic burden scores, using a modified anticholinergic burden score (mACB) (AUS) (See A1) at admission and discharge. Phone surveys of community pharmacists were conducted at three months after discharge to measure PIMs, numbers of medications, and to calculate the anticholinergic burden scores. In addition, severity and impact scores of prescribed medications were measured using the scoring system by Overhage and Lukes, as reported by Perez-Moreno et al [16] to evaluate the potential impact of the prescribing error and the effect on the patient's health. Errors were scored using five categories of severity ranging from no error, to potentially lethal. Clinical relevance of the pharmacist recommendations (impact) were scored using six likely consequences in patient care, ranging from injurious to extremely significant.

General practitioner acceptance of pharmacist recommendations following home medication review at three months after discharge was also measured using a post discharge phone call by the study pharmacist.

The intervention comprised seven strategies delivered after admission and prior to discharge (see box).

Safe Medication Strategies (SMS) Intervention

After Admission

- 1 Hospital pharmacist medication reconciliation of PWD medications on admission
- 2 Hospital pharmacist communication with carer/RACF about patient's medications
- 3 Carer needs assessment by study nurses (not applicable if admitted from RACF)

Prior to Discharge

- 4 Hospital pharmacist medication reconciliation of PWD medications at discharge, and training of patient/carer on use of medication dose administration aids (DAA) for assisted/self-medication prior to discharge (not applicable if being discharged to RACF)
- 5 Arrangements made for Medication DAA on discharge
- 6 Medication on Discharge List provided with explanation and instructions to Carer and Patient/RACF.
- 7 Contact GP about discharge medications including changes, and recommend to GP to arrange Home Medicines Review (HMR) or RMMR by Accredited Community Pharmacist

Sample size calculations were based on the primary aim (treatment effect for readmissions/re-presentation to ED). The evaluations of medication use within the study reported in this paper are secondary outcomes; consequently, sample size calculations were not performed for these outcomes. Discharge and three month data collection was not performed if consent was withdrawn, or the participant died prior to that timepoint.

Statistical analysis

Polypharmacy was defined as ≥ 5 medications. Medication recommendation severity scores were dichotomised as "Significant (severity)" Yes (1, 2, 3) and No (4, 5), and also as due to Error (1,2,3,4) and Not due to Error (5); impact scores were dichotomised as "Relevant (impact)" Yes (1, 2, 3) and No (4, 5, 6) [16].

Descriptive statistics were summarised by phase and site using means (SD) and median (min, max) for continuous data, and counts and percentages for categorical data. The change in medication use and medication reconciliation was examined from admission to discharge, and from discharge to 3 months across sites and phases using mixed modelling (negative binomial, logistic, and linear mixed modelling as appropriate). Fixed effects included phase, site, time (categorical), all two-way interactions, and a 3-way interaction term (phase*site*time), and (given adequate response numbers) included PWD characteristics identified as being potentially unbalanced between the sites (age, gender, discharge destination). A random effect was included for participant to account for correlations within a person over time. The correlations between change in number of PIMs and mACB score (admission to discharge, and discharge to 3 months) were examined (averaged over site and phase) using Spearman correlation.

The treatment effect for mean count of medication recommendations (per participant) at admission was analysed using negative binomial regression. A zero-inflated negative binomial regression model was used to examine the treatment effect for "Significant (severity)" medication recommendations, medication recommendations not due to error, and "Relevant (impact)" medication recommendations; the odds of having at least one medication recommendation was modelled together with the average count of medication recommendations in participants who had at least one medication recommendation. Modelling included phase, site, and the interaction term (phase*site), and adjusted modelling included age, gender, and number of medications at admission.

The proportion of medication recommendations classed as "Significant (severity)", as not due to error, and as "Relevant (impact)" at admission was compared across phase and site using logistic mixed modelling; modelling included phase, site, and the interaction term (phase*site), and adjusted modelling included age, gender, and number of medications at admission. A random effect was included for participant to account for correlations within a person over multiple medication recommendations.

Study data were collected and managed using REDCap (Research Electronic Data Capture) tools [18] hosted at the Hunter Medical Research Institute, Australia. Data were analysed using SAS v9.4 (SAS Institute Inc. Cary, NC); *a priori*, $p < 0.05$ (two-tailed) was used to indicate statistical significance.

Results

The final sample comprised 278 participants for the pre-intervention and 350 participants for the post-intervention phase. Patient characteristics by site and phase are presented in Table 1. There were some differences in gender, age and indigenous admissions between study sites and phases. For admissions from home, only 66% were discharged to home (343/523). Discharges to residential aged care facilities (RACF) increased by 69% compared with admissions from RACF (105 vs 178), and 5.1% died during the index admission.

Table 1
Patient characteristics, by phase and site

		Phase1 Control site	*Phase1 Intervention site*	*Phase2 Control site*	*Phase2 Intervention site*	*Total*
Characteristic Class/Statistic		*(n = 117)*	*(n = 161)*	*(n = 172)*	*(n = 178)*	*(N = 628)*
Gender Male		66 (56%)	73 (45%)	98 (57%)	73 (41%)	310 (49%)
Female		51 (44%)	88 (55%)	74 (43%)	105 (59%)	318 (51%)
Age mean (SD)		83 (7)	86 (7)	82 (8)	84 (8)	84 (8)
Aboriginal and/or TSI Yes		2 (1.7%)	1 (0.6%)	10 (5.8%)	3 (1.7%)	16 (2.6%)
Missing		1	0	0	1	2
CCI mean (SD)		2 (2)	2 (2)	2 (2)	2 (2)	2 (2)
CCI group 0		23	33	35	49	140
		(20%)	(21%)	(20%)	(28%)	(22%)
1–2		62	89	87	89	327
		(53%)	(56%)	(51%)	(51%)	(52%)
3–4		22	22	34	26	104
		(19%)	(14%)	(20%)	(15%)	(17%)
5+		10	16	15	12	53
		(8.5%)	(10%)	(8.8%)	(6.8%)	(8.5%)
Missing		0	1	1	2	4
Admitted from Home		97 (83%)	125 (78%)	149 (87%)	152 (85%)	523 (83%)
RACF		20 (17%)	36 (22%)	23 (13%)	26 (15%)	105 (17%)
Discharge destination	Home (GP)	68 (59%)	80 (50%)	98 (57%)	100 (56%)	346 (55%)
	RACF	27 (23%)	57 (36%)	42 (24%)	52 (29%)	178 (29%)
	Transitions program	1 (0.9%)	2 (1.3%)	3 (1.7%)		6 (1.0%)
	Transfer to other Acute Care Facility	15 (13%)	14 (8.8%)	14 (8.1%)	6 (3.4%)	49 (7.9%)

		Phase1 Control site	*Phase1 Intervention site*	*Phase2 Control site*	*Phase2 Intervention site*	*Total*
	Rehabilitation Facility			7 (4.1%)	4 (2.2%)	11 (1.8%)
	Died during index admission	3 (2.6%)	6 (3.8%)	8 (4.7%)	15 (8.5%)	32 (5.1%)
	Missing	3	2	0	1	6
CCI: Charlson Comorbidity Index TSI: Torres Strait Islander						

Descriptive data for medications are presented in Table 2 by phase, site and timepoint.

Table 2
Medications, by phase and site, and timepoint.

Characteristic	*Timepoint*	*Class/Statistic*	*Phase1 Control (n = 117)*	*Phase1 Intervention (n = 161)*	*Phase2 Control (n = 172)*	*Phase2 Intervention (n = 178)*	*Total (N = 628)*
Number of medications	Admission	mean (SD)	12 (5)	11 (4)	14 (5)	13 (5)	13 (5)
		median (min, max)	12 (2, 27)	11 (1, 21)	13 (1, 28)	14 (1, 33)	12 (1, 33)
		Missing	1	0	0	0	1
	Discharge	mean (SD)	10 (4)	9 (4)	10 (4)	9 (4)	9 (4)
		median (min, max)	10 (2, 20)	8 (1, 20)	10 (2, 25)	9 (1, 28)	9 (1, 28)
		Missing	10	10	21	20	61
	3 month	mean (SD)	11 (4)	9 (4)	10 (4)	9 (4)	9 (4)
		median (min, max)	10 (2, 22)	9 (2, 20)	9 (2, 21)	8 (1, 28)	9 (1, 28)
		Missing	31	50	43	49	455
Polypharmacy	Admission	Yes	110 (95%)	150 (93%)	169 (98%)	168 (94%)	597 (95%)
		Missing	1	0	0	0	1
	Discharge	Yes	99 (93%)	133 (88%)	139 (92%)	141 (89%)	512 (90%)
		Missing	10	10	21	20	61
	3 month	Yes	83 (97%)	103 (93%)	117 (91%)	111 (86%)	414 (91%)
		Missing	31	50	43	49	173
PIMs prescribed	Admission	Yes	116 (100%)	154 (96%)	171 (99.4%)	176 (99%)	617 (98%)
		Missing	1	0	0	0	1
	Discharge	Yes	106 (99.1%)	138 (91%)	148 (98%)	148 (94%)	540 (95%)
		Missing	10	10	21	20	61
	3 month	Yes	85 (99%)	107 (96%)	124 (96%)	118 (91%)	434 (95%)
		Missing	31	50	43	49	173
Number of PIMs	Admission	mean (SD)	4 (2)	4 (2)	5 (2)	4 (2)	4 (2)

Characteristic	*Timepoint*	*Class/Statistic*	*Phase1 Control (n = 117)*	*Phase1 Intervention (n = 161)*	*Phase2 Control (n = 172)*	*Phase2 Intervention (n = 178)*	*Total (N = 628)*
		median (min, max)	4 (1, 10)	3 (0, 11)	5 (0, 17)	4 (0, 11)	4 (0, 17)
		Missing	1	0	0	0	627
	Discharge	mean (SD)	4 (2)	3 (2)	4 (2)	3 (2)	3 (2)
		median (min, max)	4 (0, 9)	3 (0, 8)	4 (0, 10)	3 (0, 8)	3 (0, 10)
		Missing	10	10	21	20	567
	3 month	mean (SD)	4 (2)	3 (2)	4 (2)	3 (2)	4 (2)
		median (min, max)	4 (0, 10)	3 (0, 8)	4 (0, 9)	3 (0, 9)	3 (0, 10)
		Missing	31	50	43	49	455
MACB total score	Admission	mean (SD)	3 (2)	2 (2)	3 (2)	3 (2)	3 (2)
		median (min, max)	3 (0, 9)	2 (0, 15)	3 (0, 15)	3 (0, 10)	2 (0, 15)
		Missing	1	0	0	0	627
	Discharge	mean (SD)	3 (2)	2 (2)	3 (2)	2 (2)	2 (2)
		median (min, max)	2 (0, 10)	2 (0,10)	2 (0, 9)	2 (0, 8)	2 (0, 10)
		Missing	10	10	21	20	567
	3 month	mean (SD)	3 (2)	2 (2)	3 (2)	2 (1)	2 (2)
		median (min, max)	3 (0,10)	2 (0, 7)	2 (0, 10)	2 (0, 5)	2 (0, 10)
		Missing	31	50	43	49	455

Polypharmacy was high overall, with an average of 95% at admission, decreasing to 90% at discharge. Adjusting for age, gender and discharge destination, there were no significant differences in these proportions across sites and phases for both time points (admission to discharge p = 0.282, discharge to 3 months p = 0.894). See supplementary tables A and B.

Overall, participants were prescribed four less medications (approximately 30%) at discharge and this was sustained at three months after discharge. Overall 95–98% of participants were prescribed PIMs across timepoints. All sites showed a significant decrease in the mean number of PIMs from admission to discharge. After adjusting for age, gender and discharge destination, there was no significant treatment effect for PIMs at

admission compared to discharge ($p = 0.366$), or at discharge compared to three months ($p = 0.391$). See supplementary tables C and D.

The mean mACB score decreased for all phase/site combinations from admission to discharge, however, no treatment effect was seen ($p = 0.086$). The mean mACB score increased from discharge to 3 months at the control site in both phases, and did not change significantly at the intervention site. See supplementary tables E and F.

Averaged over site and phase, significant moderate positive correlations were seen between PIMs change and mACB change from admission to discharge ($rho = 0.48$ $p < 0.001$), and from discharge to three months ($rho = 0.55$ $p < 0.001$).

Psychotropic and Sedative/Hypnotic PIMs categories are shown in Table 3 by site and phase, and timepoint.

Table 3
PIMS, by phase and site, and timepoint

Characteristic	*Timepoint*	*Class/ Statistic*	*Phase1 Control (n = 117)*	*Phase1 Intervention (n = 161)*	*Phase2 Control (n = 172)*	*Phase2 Intervention (n = 178)*	*Total (N = 628)*
Psychotropic medication	Admission	No	63 (54%)	102 (63%)	99 (58%)	90 (51%)	354 (56%)
		Yes	53 (46%)	59 (37%)	73 (42%)	88 (49%)	273 (44%)
		Missing	1	0	0	0	1
	Discharge	No	60 (56%)	92 (61%)	86 (57%)	89 (56%)	327 (58%)
		Yes	47 (44%)	59 (39%)	65 (43%)	69 (44%)	240 (42%)
		Missing	10	10	21	20	61
	3 month	No	44 (51%)	62 (56%)	68 (53%)	70 (54%)	244 (54%)
		Yes	42 (49%)	49 (44%)	61 (47%)	59 (46%)	211 (46%)
		Missing	31	50	43	49	173
Sedative/hypnotic medication	Admission	No	97 (84%)	141 (88%)	140 (81%)	148 (83%)	526 (84%)
		Yes	19 (16%)	20 (12%)	32 (19%)	30 (17%)	101 (16%)
		Missing	1	0	0	0	1
	Discharge	No	99 (93%)	140 (93%)	139 (92%)	153 (97%)	531 (94%)
		Yes	8 (7.5%)	11 (7.3%)	12 (7.9%)	5 (3.2%)	36 (6.3%)
		Missing	10	10	21	20	61
	3 month	No	77 (90%)	95 (86%)	116 (90%)	122 (95%)	410 (90%)
		Yes	9 (10%)	16 (14%)	13 (10%)	7 (5.4%)	45 (9.9%)
		Missing	31	50	43	49	173

There were no differences in the proportion of participants on at least one psychotropic medication between sites, phases and timepoints (admission to discharge p = 0.275, discharge to three months p = 0.915). See supplementary tables G and H.

From admission to discharge, there was a significant decrease in the proportion of participants on at least one sedative/hypnotic medication at the control site in both phases and the intervention site in phase two and this is a clinically significant improvement in prescribing, however, it could not be shown that this was due to the intervention (admission to discharge p = 0.233, discharge to three months p = 0.807). See supplementary tables I and J.

Pharmacist medication reconciliation conducted at admission and prior to discharge is shown in Table 4 by site, phase and timepoint.

Table 4
Pharmacist Medication reconciliation, by phase and site, and timepoint

			Phase1 Control	***Phase1 Intervention***	***Phase2 Control***	***Phase2 Intervention***	***Total***
Characteristic	*Timepoint*	*Class/Statistic*	*(n = 117)*	*(n = 161)*	*(n = 172)*	*(n = 178)*	*(N = 628)*
Medication reconciliation	Admission	No	75 (65%)	111 (69%)	101 (59%)	1 (0.6%)	288 (46%)
		Yes	41 (35%)	49 (31%)	71 (41%)	173 (97%)	334 (53%)
		Unable to deliver				4 (2.2%)	4 (0.6%)
		Missing	1	1	0	0	2
Medication reconciliation	Discharge	No	109 (99.1%)	111 (74%)	156 (95%)	4 (2.5%)	380 (65%)
		Yes	1 (0.9%)	38 (26%)	8 (4.9%)	139 (85%)	186 (32%)
		Unable to deliver				20 (12%)	20 (3.4%)
		Missing	7	12	8	15	42

The increase in the proportion of participants receiving pharmacist medication reconciliation at admission was clinically significant in the Intervention group between phase one and phase two, while the control group remained stable (numbers too low to support regression modelling); similar was seen at discharge.

Pharmacists' recommendations for medications that were identified during medication reconciliation as having a potential for harm or adverse reaction or prescribing error, were evaluated for their severity and relevance (impact of the service provided by the pharmacist). Severity and impact scores for pharmacist's medication recommendations (per participant) are shown in table 5.

Table 5:
Medication recommendations (admission, per participant), by phase and site

Characteristic	*Class/Statistic*	*Phase1 Control (n=117)*	*Phase1 Intervention (n=161)*	*Phase2 Control (n=172)*	*Phase2 Intervention (n=178)*	*Total (N=628)*
At least 1 medication recommendation	**No**	**82 (70%)**	**135 (84%)**	**111 (65%)**	**12 (6.7%)**	**340 (54%)**
	Yes	35 (30%)	26 (16%)	61 (35%)	166 (93%)	288 (46%)
Number of recommendations	mean (SD)	1 (2)	0 (1)	1 (2)	6 (4)	2 (3)
	median (min, max)	0 (0, 10)	0 (0, 11)	0 (0, 10)	6 (0, 26)	0 (0, 26)
At least 1 Significant (Severity) medication recommendation	No	88 (75%)	143 (89%)	122 (71%)	49 (28%)	402 (64%)
	Yes	29 (25%)	18 (11%)	50 (29%)	129 (72%)	226 (36%)
Number of (Significant Severity) recommendations	mean (SD)	1 (1)	0 (1)	1 (1)	2 (2)	1 (1)
	median (min, max)	0 (0, 6)	0 (0, 4)	0 (0, 6)	2 (0, 8)	0 (0, 8)
At least 1 medication recommendation - not due to error (severity 5)	No	103 (88%)	153 (95%)	138 (80%)	27 (15%)	421 (67%)
	Yes	14 (12%)	8 (5.0%)	34 (20%)	151 (85%)	207 (33%)
Number of recommendations not due to error	mean (SD)	0 (1)	0 (1)	0 (1)	3 (3)	1 (2)
	median (min, max)	0 (0, 5)	0 (0, 11)	0 (0, 9)	3 (0, 23)	0 (0, 23)
At least 1 Relevant (Impact) medication recommendation	No	87 (74%)	143 (89%)	116 (67%)	18 (10%)	364 (58%)
	Yes	30 (26%)	18 (11%)	56 (33%)	160 (90%)	264 (42%)
Number of Relevant (Impact) recommendations	mean (SD)	1 (1)	0 (1)	1 (2)	4 (3)	2 (3)
	median (min, max)	0 (0, 5)	0 (0, 4)	0 (0, 9)	4 (0, 24)	0 (0, 24)

The proportion of participants with at least 1 medication recommendation at admission increased significantly in the Intervention group (OR 78.9, $p < 0.001$) and did not change at the control site, (OR 1.12, $p = 0.676$), and the overall effect was significant (OR 70.5, $p < 0.001$). The mean count of medication recommendations per participant increased significantly in the Intervention group between phase 1 and phase 2 (IRR 13.6, $p < 0.001$), while the control group remained stable (IRR 0.98, $p = 0.923$). See supplementary tables K and L.

Medication recommendations per participant scored as "Significant (severity)" was modelled as a 2-part model; the increase (phase 2 compared to phase 1) in the proportion of participants having at least one "Significant (severity)" medication recommendation was significantly more at the intervention site than the control site (OR 20.5 $p < 0.001$). While the mean count of "Significant (severity)" medication recommendations increased significantly in the intervention site from Phase 1 to Phase 2 (IRR 1.9 $p = 0.022$), and decreased significantly in the control site (IRR 0.6 $p = 0.006$), the mean count at the intervention site in Phase two was still lower than the mean count at the control site in Phase one. See supplementary tables M and N.

In addition, there was an increase in proportion of participants with at least one medication recommendation that was “not due to error”, at the intervention site (OR 104, $p < 0.001$) and overall (OR 65.2, $p < 0.001$). See supplementary table O.

The mean count of medication recommendations per participant scored as "Relevant (impact)" was modelled as a 2-part model; the increase in the proportion of participants having at least 1 "Relevant (impact)" medication recommendation was significantly more at the intervention site for phase 2 compared to phase 1, than the control site (OR 63.1, $p < 0.001$). The mean count per participant of "Relevant (impact)" medication recommendations increased significantly at the intervention site from Phase 1 to Phase 2 (IRR 4.5, $p < 0.001$), and this change was significantly different to the change at the control site (treatment effect IRR 4.4, $p < 0.001$). See supplementary tables P and Q.

Descriptive scores for medication recommendations (all medication recommendations, N = 1789) are shown in table 6 by site and phase.

Table 6
Medication recommendations (admission, recommendation level), by phase and site

Characteristic	*Class/Statistic*	*Phase1 Control (n=211)*	*Phase1 Intervention (n=196)*	*Phase2 Control (n=316)*	*Phase2 Intervention (n=1066)*	*Total (N=1789)*
Significant (Severity) medication recommendation	**No**	**46 (36%)**	**29 (49%)**	**102 (50%)**	**725 (69%)**	**902 (62%)**
	Yes	83 (64%)	30 (51%)	103 (50%)	329 (31%)	545 (38%)
	Missing	82	137	111	12	342
Severity of the prescription error	2. Serious	10 (7.8%)	10 (17%)	12 (5.9%)	51 (4.8%)	83 (5.7%)
	3. Significant	73 (57%)	20 (34%)	91 (44%)	278 (26%)	462 (32%)
	4. Least	19 (15%)	7 (12%)	20 (9.8%)	104 (9.9%)	150 (10%)
	5. No error	27 (21%)	22 (37%)	82 (40%)	621 (59%)	752 (52%)
	Missing	82	137	111	12	342
Relevant (Impact) medication recommendation	No	56 (43%)	32 (52%)	63 (31%)	324 (31%)	475 (33%)
	Yes	73 (57%)	29 (48%)	142 (69%)	730 (69%)	974 (67%)
	Missing	82	135	111	12	340
Impact of the service provided by the pharmacist	1. Extremely significant				3 (0.3%)	3 (0.2%)
	2. Highly significant	5 (3.9%)	11 (18%)	11 (5.4%)	99 (9.4%)	126 (8.7%)
	3. Significant	68 (53%)	18 (30%)	131 (64%)	628 (60%)	845 (58%)
	4. Little significant	15 (12%)	6 (9.8%)	10 (4.9%)	35 (3.3%)	66 (4.6%)
	5. Insignificant	40 (31%)	26 (43%)	53 (26%)	289 (27%)	408 (28%)
	6. Injurious intervention	1 (0.8%)				1 (0.1%)
	Missing	82	135	111	12	340

The proportion of medication recommendations that are "Significant (severity)" decreased significantly at the intervention site between phase 1 and phase 2 (OR 0.37 p = 0.006), although this decrease was not significantly different to the decrease seen at the control site (treatment effect OR 0.63 p = 0.328). See supplementary table R.

There was a significant increase in the proportion of medication recommendations that did not involve a prescribing error at both sites in phase two, compared to phase one (Intervention OR 3 p = 0.003, Control OR 2.4 p = 0.008), although the overall treatment effect was not significantly different (OR 1.2 p = 0.666). See supplementary table S.

There was a significant increase in the proportion of Relevant (impact of pharmacist service) recommendations at the intervention site in phase two, compared to phase one (OR 2.2 p = 0.031), although this change was not significantly different to the increase seen at the control site (treatment effect OR 1.2 p = 0.695). See supplementary table T.

A significant moderate positive correlation was seen between severity and impact of medication recommendations at admission (n = 1446, Rho = 0.58 p < 0.001).

The GP acceptance of community pharmacist's recommendations at three months after discharge was 68% (n = 104/156 recommendations).

Discussion

Polypharmacy was high overall (> 90%) and this reflects high comorbidity in this study population, and increasing comorbidity has been reported to be significantly associated with higher polypharmacy [19]. This result is higher than the rate reported in a study of older people including participants with cognitive impairment (n = 373) with a rate of 69% for polypharmacy [19] and a study that included 10,528 participants with dementia in primary care of 57% [3].

The number of medications at discharge reduced by 30% across study sites and phases and this was sustained at three months, suggesting that medication reconciliation and deprescribing is practiced to some extent in the delivery of usual care and may explain why the study was not able to report a treatment effect. Nonetheless reduced prescribing reduces medication related risk for PWD [1, 19, 20].

PIMs prescribing was very high (> 90%) overall in this study. Previous studies have reported lower rates of PIMs prescribing (of at least one PIM) for PWD in the community. A multi-country study (n = 2004) reported a rate of 60% [4] and a nationwide study (n = 2190) reported a rate of 67% [21], however a recent systematic review reported prevalence of PIMS ranged from 53–90% for inpatients with cognitive impairment [10]. The mean number of PIMs decreased significantly (by 25%) from admission to discharge and this also reduced medication related risk for PWD [1, 4], however no treatment effect was identified.

The mean mACB score decreased significantly from admission to discharge and this suggests reduced risk for PWD, however no treatment effect was identified. The significant moderate positive correlations between PIMs reduction and mACB reduction also indicate reduced medication related risk for PWD in this study.

Prescribed psychotropic medications did not vary significantly from admission, however 44% of patients were prescribed these medications. A report from Alzheimer's Australia states that up to 20% of PWD who receive antipsychotic medications derive benefit from them [22], so there is potential for inappropriate prescribing for PWD in this study.

The proportion of participants on at least one sedative/hypnotic was significantly reduced at discharge at both sites (by 60%) – this is a clinically significant improvement in prescribing because it reduces risk for PWD, however no treatment effect was identified. This reduction may have been influenced by a recent initiative by the Australian Commission on Safety and Quality in Health Care that published National Safety and Quality Health Service Standards and targeted inappropriate prescribing for BPSD (https://www.safetyandquality.gov.au/publications-and-resources/resource-library/reducing-inappropriate-use-antipsychotics-people-behavioural-and-psychological-symptoms-dementia-bpsd-infographic).

Medication reconciliation at admission and discharge increased significantly in the intervention site in phase two in this study. Medication review has been reported to significantly improve the appropriateness of prescribing in aged care facilities [14, 15] and primary health care [13].

There was a significant increase in the mean number of medication recommendations identified by pharmacists during medication reconciliation at the intervention site in phase two. There was a high proportion of participants in the intervention group who received at least one medication recommendation (93%) and this was higher than the proportions for usual care/phase 1 participant groups (16–35%). This result is higher than the rate (19%) reported in an observational study (n = 2984) of admissions to emergency department (ED) [16], and may indicate that PWD require more modifications of their medications.

There was a significant increase in the proportion of participants having at least one "Significant (severity)" medication recommendation for the intervention group (72%) compared with the usual care groups (21%). Increased severity scores for the intervention group may have patient safety implications or may be the result of increased medication reconciliation at admission. The observational ED study reported a rate of 57% of significant severity recommendations [16].

The proportion of patients having at least one medication recommendation not due to error increased significantly at the intervention group (85%) compared with the usual care/phase 1 groups (5–20%). This suggests that pharmacists may have recommended modifications in medications rather than flagging potential drug interactions or adverse effects.

There was a significant increase in the proportion of participants having at least one relevant pharmacist medication recommendation in the intervention group (90%), indicating a clinically significant impact of the service provided by the pharmacist. The usual care/phase 1 rates ranged from 11–33% and these were lower than the rate reported in the previous ED study (65%) [16]. The significant moderate positive correlation between severity and impact scores in this study was similar to the correlation reported in the previous ED study (Rho = 0.73 $p < 0.001$) [16].

The significant severity scores (by number of medication recommendations) were significantly lower at the intervention site in phase two compared with the control site in phase one. However, there was variation between

the sites in phase one, and between the phases at the control site, and this finding should be interpreted and extrapolated cautiously.

The proportion of medication recommendations that were not due to error (by number of medication recommendations) increased significantly at the intervention site between phase one and two, however no treatment effect was identified.

There was a significant increase in the relevance (impact) of medication recommendations (by number of medication recommendations) at the intervention site between phase one and two, however no treatment effect was identified.

GP acceptance of at least one HMR recommendation at three months after discharge was 68%, and this was higher than an observational study in primary care (n = 91) in which GP acceptance of 304/625 pharmacist recommendations (48%) was reported [13], and a study (n = 1021) reporting GP acceptance of ED pharmacist recommendations (49%) [23].

Previous studies have reported the effect of interventions on medication safety for older people in the community or primary care settings [12–15], however this study evaluated the effectiveness of a pharmacist intervention for PWD inpatients and the effect on polypharmacy and PIMS. Medication safety for PWD is particularly important because of the risks associated with medications for PWD. The Australian Health Ministers Advisory Council has established nine National Health Priority Areas, including dementia, and in 2019 they announced that quality use of medicines and medicine safety will be the 10th National Health Priority Area in Australia (https://vivacommunications.com.au/blog/medicines-safety-now-a-national-health-priority/). The addition of this priority area should emphasize the importance of this issue for future research and practice improvement initiatives.

Clinical Implications

PWD or cognitive impairment are not always identified at admission. Consequently, clinicians may not recognise that this vulnerable group of patients needs particular attention regarding their medications. PWD often have polypharmacy and many associated medication safety concerns. Polypharmacy may be a consequence of their complex comorbidities. Pharmacist-led medication reconciliation is a valuable means of ensuring medication safety for PWD and can result in them having improved outcomes due to reductions in polypharmacy, PIMs and deprescribing.

Strengths and Limitations:

Few previous studies have been conducted exclusively on PWD in acute care and focused on their medication safety. PWD or cognitive impairment is not always identified at admission. Having an intervention that focuses on PWD in an inpatient setting requires robust systems for identification of PWD that are sensitive to their needs and values. This study undertook screening to identify PWD at admission, and evaluated the effect of a pharmacist-led intervention on polypharmacy and PIMs for PWD in acute care. The study design only used two sites and participants were not randomised, and this limits the internal validity and generalisability of the

results. In addition, values of all regression findings should be interpreted cautiously due to low numbers and only two study sites.

Conclusions

This study has identified that admission to hospital presents an opportunity to undertake medication reconciliation and minimise risk for medication related poor outcomes for PWD. Medication reconciliation can contribute to reducing polypharmacy and PIMs and result in recommendations for improved medication safety, due to identifying potential drug interactions, side effects, dosage modifications, and deprescribing. This study highlights the need for focused medication management in this high risk population. The results indicate that the intervention is feasible to implement and is helpful to informing future multisite studies that would have sufficient power to demonstrate treatment effect.

Abbreviations

SMS; Safe Medication Strategy; PWD: People with dementia; PIM: Potentially inappropriate medication; RACF: Residential aged care facility; ED: Emergency department; mACB (AUS): modified Anticholinergic Cognitive Burden Scale (Australia); HREC: Human Research Ethics Committee; BPSD: Behavioural and Psychological Symptoms of Dementia; GP: General Practitioner.

Declarations

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Author Contributions

SF was responsible for project management, data collection and management, delivery of the intervention, and drafting, reviewing and editing of the manuscript.

AF was an investigator and contributed to funding acquisition, participated in design of the study and study instruments, data scoring, and review and editing of the manuscript.

CH was an investigator and contributed to funding acquisition, participated in the design of the study and contributed to manuscript development and revisions.

KP was responsible for software management, database construction, data analysis and drafting, reviewing and editing the manuscript.

CO was an investigator and contributed to funding acquisition, participated in the design of the study, software management and data analysis, and contributed to manuscript development and revisions

DP was an investigator and contributed to funding acquisition, participated in the design of the study, and contributed to manuscript development and revisions.

AS was an investigator and contributed to funding acquisition, participated in the design of the study, and contributed to manuscript review and editing.

RL contributing to manuscript review and editing.

RB and WM contributed to data collection, delivery of the intervention, and reviewing and editing of the manuscript.

JA was an investigator and contributed to funding acquisition, participated in the design of the study, and contributed to manuscript review and editing.

AK was the lead investigator and responsible for funding acquisition, participated in the design and coordination of the study and design of study instruments, contributed to data collection and analysis, and drafted the manuscript.

The SMS Dementia Study investigators include: A.K., C.H., J.A., C.O., D.P., A.F., A.S., K.P., R.L., S.F., R.B., and W.M. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and analysed during this study are not available to readers, because the investigators do not have permission from participants to make the data available. However, the study team would be pleased to be contacted by any research groups that may be interested in collaborating on future work.

Ethics Approval and Consent to Participate

This study was approved by the Hunter New England Health Human Research Ethics Committee (HREC) (17/06/21/4.08) and University of Newcastle (Australia) HREC (H-2017-0260). All participants had written consent provided by their carer or person responsible prior to their participation in the study.

Consent for Publication

Not applicable

Competing Interests

The authors declare that they have no competing interests.

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Additional Files

Figure A1: Modified Anticholinergic Burden Score (mACB) (AUS).

Supplementary Tables.

Supplementary Files

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- FigureA1.docx
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