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Trajectories of pro re nata (PRN) medication prescribing and administration in long-term care facilities

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Declaration of Interest

JKS was an embedded researcher within Helping Hand Aged Care during 2017-19. MC and MH report employment by Helping Hand Aged Care in the last 36 months. JSB and JKS report grant funding from Resthaven Inc. and the Australian Government Aged Care Quality Agency in the last 36 months.

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Abstract

Background: Little is known about changes in *pro re nata* (PRN) medication prescribing and administration in residential aged care facilities (RACFs) over time.

Objective: To determine the prevalence and factors associated with PRN medication administration in RACFs and examine changes over 12-months.

Methods: Secondary analyses utilizing data from the SIMPLER randomized controlled trial (n=242 residents, 8 RACFs) was undertaken. PRN medication data were extracted from RACF medication charts. Factors associated with PRN medication administration in the preceding week were explored using multivariable logistic regression.

Results: At baseline, 211 residents (87.2%) were prescribed ≥1 PRN medication, with 77 (36.5%) administered PRN medication in the preceding week. PRN administration was more likely in non-metropolitan areas, and less likely among residents with more severe dementia symptoms and greater dependence with activities of daily living. No significant differences in overall PRN prescribing or administration in 162 residents alive at 12-month follow-up were observed.

Conclusions: Despite being frequently prescribed, the contribution of PRNs to overall medication use in RACFs is small. PRN prescribing and administration was relatively static over 12-months despite likely changes in resident health status over this period, suggesting further exploration of PRN prescribing in relation to resident care needs may be warranted.

Keywords

Pro re nata; nursing homes; long-term care; residential aged care; medication administration; medication management.

Introduction

Pro re nata (PRN or as needed) medications comprise one-third to one-half of all medications prescribed in residential aged care facilities (RACFs) and are administered in response to acute episodes (e.g. chest pain) or for conditions with fluctuating symptoms (e.g. constipation).[1-3] A recent systematic review reported 48.4% to 97.4% of residents are prescribed PRN medication (n=7 studies).[2] However, most existing studies were published >20 years ago and largely focus on PRN prescribing,[2] with the frequency of administration not extensively researched. Evidence from one study suggested 28% of residents are administered PRN medication each week, while another study reported an average of 5.85 PRN administrations per person-month.[4, 5]

Improved understanding the frequency of PRN medication administration is needed as RACF nurses often make the decision to administer PRNs that are prescribed by general medical practitioners (GPs). When prescribed and administered appropriately, PRN medications provide residents with timely access to medications for symptom management. However, safety concerns have been raised about recognition and management of possible adverse events post-administration and the risk of exceeding the maximum recommended dose when the same medication is given PRN and regularly.[3-6] Although existing studies suggest it is rare to exceed the maximum daily dose for this reason,[4, 5] nervous system medications that are commonly administered PRN may pose safety concerns at high doses.

PRN prescribing might change during an individual's RACF stay. Reduced mobility and functional decline over time may increase pain and impact utilization of regular and/or PRN opioids and laxatives.[7] Medications targeted for deprescribing in RACFs may be prescribed PRN for short periods,[8] while PRN medications that are administered frequently may be re-charted for regular administration. Death is the most common reason for exiting an RACF[9] and administration of PRN opioids, benzodiazepines and antiemetics is noted to be increased at end-of-life.[4, 10] Conducting longitudinal studies to determine medication use trajectories is an international priority area for geriatric

pharmacotherapy research.[11] Despite this, little is known about changes in PRN medication prescribing and administration in RACFs over time.

This study examined the prevalence and resident characteristics associated with the administration of PRN medications and explored changes in PRN prescribing and administration over 12-months.

Methods

Design, setting and participants

Secondary analyses of baseline and 12-month follow-up data from the SImplification of Medications Prescribed to Long-tErm care Residents (SIMPLER) cluster randomized controlled trial were conducted. SIMPLER received ethical approval from [university name] and has been described elsewhere.[12, 13] Briefly, English-speaking permanent residents who took ≥1 medication regularly were recruited from 8 South Australian RACFs in 2017. Similar to long-term care facilities, RACFs provide accommodation and personal care for individuals who can no longer stay at home.[1] Residents anticipated to live for <3 months were excluded from participating at baseline. Of the 720 residents screened, 631 were invited to participate and informed consent was obtained for 242 individuals.

Medication data

Exposures of interest were the prevalence of PRN prescribing and administration at baseline and follow-up, and PRN administrations in the previous 24-hours and 7 days. Details for all prescription and non-prescription medications (e.g. multivitamins, complementary and alternative medications) were extracted from paper-based medication charts and coded using the World Health Organization Anatomical Therapeutic Chemical (ATC) Classification System.[14] Nurse-initiated medications, telephone

orders, medications prescribed on the short-term section (e.g. antibiotics) and non-medications (e.g. bandages) were excluded. Prescriptions for different formulations of the same medication were considered as separate prescriptions. For all medications prescribed PRN, we determined the total number of doses of the same medications administered regularly over the preceding week and calculated the proportion of administrations that were for PRN medications. Among residents who were administered a PRN medication in the 24-hours pre-study entry, we reviewed regularly prescribed medications and calculated the total dose administered over that 24-hour period and compared to the maximum recommended dose.[15, 16]

Covariates

Research nurses collected baseline demographic information and administered the following scales: the Katz activities of daily living (ADL),[17] FRAIL-NH,[18] Dementia Severity Rating Scale (DSRS)[19] and Mini Nutritional Assessment Short Form.[20] Disease burden was characterized using the Charlson Comorbidity Index.[21] Loss to follow-up was recorded over 12-months.

Analysis

Resident characteristics associated with PRN medication administration among individuals charted ≥1 PRN medication at baseline were examined using logistic regression. Variables with a p-value of ≤0.25 in the univariate models were eligible for inclusion in a backward stepwise multivariate logistic regression analysis.

Wilcoxon signed rank and McNemar's tests were used to investigate prescribing changes at 12-months. Residents from both SIMPLER study arms were included because the intervention delivered in

SIMPLER aimed to consolidate administration times for regular medications and did not target deprescribing nor PRN medications.[12, 13] Data were analyzed using SAS v 9.4 (SAS Institute, Cary, NC).

Results

Baseline characteristics of the 242 residents are summarized in Table 1. At baseline, 2280 medications were prescribed for regular administration and 1090 for PRN administration. This included 29 PRN medications prescribed for resident self-administration. Residents were prescribed a median of 4 (IQR 2-6) PRN medications. There were 211 (87.2%) residents prescribed PRN medication, although considerable intra-facility variation in prescribing was observed, ranging from 33.3% to 97.3% across the 8 RACFs (Figure 1). The distribution of medications prescribed regularly, regularly and PRN, and only PRN across each therapeutic class is summarized in Figure 2 and Table 2. The most prevalent PRN medications prescribed were paracetamol (54.1% of residents), docusate and sennosides (40.9%) and metoclopramide (26.8%).

Of the 211 residents prescribed PRN medication, 25 (11.8%) were administered ≥1 PRN medication in the 24-hours before study entry (n=32 administrations) and in these individuals there were no instances where the maximum daily dose recommended for that medication was exceeded. Additionally, 77 (36.5%) residents were administered ≥1 PRN medication in the week before study entry, with administration rates of 22.2% to 88.9% across the RACFs (Figure 1). Among these 77 residents, the median number of PRN medications administered in the week pre-study entry was 1 (IQR 1-2) and the median number of administrations was 2 (IQR 1-3). Laxatives and opioids were the most commonly administered PRNs (Table 2). PRN administrations accounted for 0.9% of all medication administrations.

In the final multivariable model, PRN administration was more likely among individuals residing in a regional area and less likely among individuals with higher DSRS and Katz ADL scores (Table 1).

Among the 162 residents alive at follow-up, no significant change in the total number of medications prescribed at baseline and follow-up were observed for medications prescribed regularly (median 9 (IQR 7-12) vs. 9 (IQR 6-12), p=0.055) or PRN (4 (IQR 2-6) vs. 4 (IQR 2-7), p=0.216). No significant changes in overall prevalence of PRN prescribing were observed at follow-up (87.7% vs. 93.2%, p=0.095) although small increases in PRN antipsychotic prescribing occured (Supplementary Table 1). The proportion of residents administered PRN medication in the preceding week was similar at follow-up (32.4% vs. 28.5%).

Discussion

The main study findings were that almost 9 in every 10 residents were prescribed PRN medication, with nervous system and alimentary tract and metabolism medications frequently prescribed. Administration was less common, with 37% receiving PRN medication over a 7-day period and a median of 2 PRN doses administered, although facility-level variation was observed. PRN administration was more likely in non-metropolitan locations and less likely among individuals with more severe symptoms of dementia or greater dependence with ADLs. The overall number of medications prescribed did not change considerably over time.

This high prevalence of PRN prescribing is consistent with existing evidence suggesting 48-97% of residents are prescribed PRN medication.[2, 4, 5, 22] This may reflect anticipatory prescribing to optimize resident care and limit unnecessary hospitalizations in accordance with current guidelines[23] and/or the model of primary care delivery in the RACF. In Australia, GPs visit RACFs periodically but are often based off-site[24] and PRNs may be prescribed to ensure residents and staff have timely access to

medications for symptom management. Factors impacting the high PRN prescribing rates observed could be further explored among stakeholders using a qualitative approach. The PRN administration rates observed in this study are consistent with a previous South Australian study that reported 28% of residents were administered a PRN medication over 7 days, with administration more likely among residents with a greater dependence with ADLs and taking more medications regularly.[5] Associations between greater dementia severity and PRN medication administration in the present study may reflect difficulty in communicating symptoms but requires further exploration to identify whether differences in regular medication prescribing also exist. Our findings contrast with another Australian study which reported a three-fold variation in PRN administration rates was observed across RACFs over 12-months that was not explained by resident age nor dementia diagnosis.[4]

Alimentary tract or nervous system medications were often prescribed for both regular and PRN administration, and PRN administration was generally sparse. This suggests a preference to treat conditions such as pain and constipation using medications administered regularly rather than PRN. Australian guidelines recommend regular administration of paracetamol as a first-line analgesic and routine prescription of laxatives when prescribing opioids.[15, 23] Although residents were often prescribed medications from the same class both regularly and PRN, there was no evidence that maximum doses were exceeded when a PRN medication was administered. This is an encouraging finding because supratherapeutic doses can occur when the same medications are prescribed regularly and PRN.[3, 6]

Overall, PRN prescribing or administration did not change considerably over time. This finding may have been influenced by baseline length of stay, the modest sample size or because residents who died during follow-up were excluded. Previous cross-sectional studies have reported conflicting associations between length of stay and number of PRN medications prescribed.[2, 4, 5, 22, 25] Changes in PRN prescribing and administration might be more prevalent at RACF entry or end-of-life. A recent

study reported PRN medications were administered more frequently to residents who died during 12-month follow-up compared to those alive (mean 8.0 versus 5.0 administrations per person-month).[4]

Small increases in PRN antipsychotic prescribing were observed at follow-up, despite Australian guideline recommendations for antipsychotics prescribed for behavioral symptoms in residents with dementia to be reviewed within three months.[23, 26] Factors such as the model of primary care delivery and regular medication reviews could impact use of high-risk medications for extended durations. Decreases in PRN and regular opioid and benzodiazepine prescribing were observed post-collaborative medication review in Norwegian RACFs,[27] while the presence of an in-house GP facilitated a reduction in the mean percentage of residents prescribed a PRN (75% to 68%, $p<0.001$) in a recent Australian trial.[28]

While frequently prescribed, PRN medications accounted for only 7% of opioid and 5% of anxiolytic administrations. The inability to discern between medications dispensed for regular and/or PRN use is a common limitation of RACF pharmacoepidemiological studies using pharmacy claims data to determine medication exposure. Our finding that PRNs comprised <1% of all administrations over 7-days, and that prescribing and administration did not change considerably during follow-up, provides further reassurance that the contribution of PRN medications to total medication exposure in RACF-based studies is likely to be small.

Strengths and limitations

This study utilized comprehensive data from RACFs maintained by the same not-for-profit provider. Participants were similar to all individuals receiving residential care from this provider and the wider Australian RACF population in terms of age, sex and dementia diagnosis.[12, 29] However, study findings may not reflect practices in all RACFs or end-of-life care. Provision of non-pharmacological

interventions, discussions about PRN use with the prescriber, and/or resident outcomes post-PRN administration are unknown. Administration among 10 residents self-administering may be underestimated as no PRN administrations were recorded for those individuals. We were also unable to determine the appropriateness of prescribing or whether PRN medications were under-administered.

Conclusions

Approximately one third of residents are administered a PRN medication each week. There is little variation in PRN prescribing or administration over time and the overall contribution to total medication use in RACFs is small. Further exploration of PRN prescribing in relation to changing resident care needs may be warranted, along with future research to understand non-pharmacological interventions undertaken before PRN administration and utilization in specific situations such as end-of-life care.

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249 **Table 1**. Characteristics of all participating residents (n=242) and those associated with *pro re nata*
250 (PRN) medication administration in the week prior to study entry among residents prescribed PRN
251 medication (n=211)

Characteristic	**Median (IQR) or N (%) at study entry (n=242 residents)**	**Univariate analysis[a]**		**Multivariate analysis[a,b]**	
		Odds ratio (95% CI)	**p-value**	**Adjusted odds ratio (95% CI)**	**p-value**
Age in years	87.0 (81.0-92.0)	1.01 (0.97-1.04)	0.805		
Female	179 (74.0%)	0.93 (0.49-1.77)	0.828		
Rural location	48 (19.8%)	2.93 (1.28-6.70)	0.011	3.01 (1.26-7.19)	0.013
Length of RACF stay (years)	2.5 (1.0-4.7)	1.03 (0.94-1.13)	0.499		
Charlson Comorbidity Index score	2.0 (2.0-3.0)	1.05 (0.88-1.27)	0.549		
Dementia diagnosis	131 (54.1%)	0.56 (0.32-0.99)	0.046		
Dementia Severity Rating Scale score[c]	21.0 (11.5-38.5)	0.99 (0.97-1.01)	0.239	0.95 (0.93-0.98)	<0.001
Mini Nutritional Assessment Short Form (MNA-SF)	9.5 (8.0-11.0)	0.93 (0.83-1.04)	0.197		
Katz Activities of Daily Living score	1.0 (1.0-3.0)	0.84 (0.71-0.98)	0.029	0.65 (0.52-0.81)	<0.001
Frailty in Nursing Homes (FRAIL-NH) score[c]	7.0 (3.0–10.0)	1.10 (1.02-1.18)	0.010		

No. of medications charted for regular administration	9.0 (6.0-12.0)	1.08 (1.01-1.15)	0.020		

252 CI confidence interval; IQR interquartile range; RACF residential aged care facility
253 [a]among residents prescribed at least one PRN medication at baseline
254 [b]Hosmer and Lemeshow goodness-of-fit test p=0.626
255 [c]Not recorded for n=2 residents

256 **Table 2**. *Pro re nata* (PRN) medication prescribing and administration at baseline (n=242 residents)

Medication name/class (ATC code)	**Medications prescribed (n, %)**		**PRN medication administered in the previous 7 days**		**Percentage of all administrations in the previous week that were PRN**
	Prescribed PRN (n, %)	**Prescribed for administration regularly (n, %)**	**N (%)**	**No. of PRN administrations, median (IQR)**	
Alimentary tract and metabolism (A)	180 (74.4)	219 (90.5)	37 (20.6)	1.0 (1.0-1.0)	1.6
Blood and blood forming organs (B)	4 (1.7)	148 (61.2)	-	-	-
Cardiovascular system (C)	37 (15.3)	169 (69.8)	2 (5.4)	1.0 (1.0-1.0)	0.1
Dermatologicals (D)	48 (19.8)	55 (22.7)	2 (4.2)	3.5 (1.0-6.0)	0.7
Genito Urinary System (G)	7 (2.9)	39 (16.1)	-	-	-
Systemic Hormonal Preparations (H)	9 (3.7)	45 (18.6)	-	-	-
Antiinfectives (J)	1 (0.4)	20 (8.3)	-	-	-
Musculo-skeletal system (M)	25 (10.3)	82 (33.9)	3 (12.0)	1.0 (1.0-1.0)	0.4
Nervous System (N)	197 (81.4)	217 (89.7)	42 (21.3)	2.0 (1.0-3.0)	1.5
Respiratory System (R)	65 (26.9)	51 (21.1)	6 (9.2)	2.0 (1.0-3.0)	1.6

Sensory Organs (S)	19 (7.9)	73 (30.2)	1 (5.3)	-	0.2
Specific medication classes					
Antacids (A02A)	26 (10.7)	4 (1.6)	1 (3.8)	1.0 (1.0-1.0)	1.8
Propulsives (A03FA)	67 (27.7)	3 (1.2)	1 (1.5)	1.0 (1.0-1.0)	2.3
Laxatives (A06)	166 (68.6)	124 (51.2)	33 (19.9)	1.0 (1.0-2.0)	3.7
Loperamide (A07DA03)	31 (12.8)	1 (0.4)	1 (3.2)	12 (12.0-12.0)	77.4
Organic nitrates (C01DA)	27 (11.1)	16 (6.6)	-	-	-
Dermatological corticosteroids (D07)	42 (17.3)	16 (6.6)	2 (4.8)	3.5 (1.0-6.0)	3.6
Opioids (N02A)	90 (37.2)	73 (30.2)	20 (22.2)	2.0 (1.0-2.5)	7.1
Paracetamol (N02BE01, N02AJ06)	131 (54.1)	156 (64.5)	9 (6.9)	3.0 (2.0-4.0)	0.9
Antipsychotics (N05A*)	23 (9.5)	55 (22.7)	2 (8.7)	2.5 (2.0-3.0)	0.8
Anxiolytics (N05B)	64 (26.4)	34 (14.0)	9 (14.1)	1.0 (1.0-2.0)	4.9
Hypnotics & Sedatives (N05C)	34 (14.1)	27 (11.2)	4 (11.8)	1.0 (1.0-1.50)	2.6
Salbutamol (R03AC02)	51 (21.1)	12 (5.0)	2 (3.9)	1.0 (1.0-1.0)	0.9

*excluding lithium and prochlorperazine

259 **Figure legends**

260 Figure 1. Boxplot of facility-level variation in pro re nata (PRN) medication prescribing and

261 administration (n=8 facilities)

262 Figure 2. Prevalence of prescribing of *pro re nata* (PRN) and regular medications at study entry

263

Figure 1. Boxplot of facility-level variation in *pro re nata* (PRN) medication prescribing and administration (n=8 facilities)

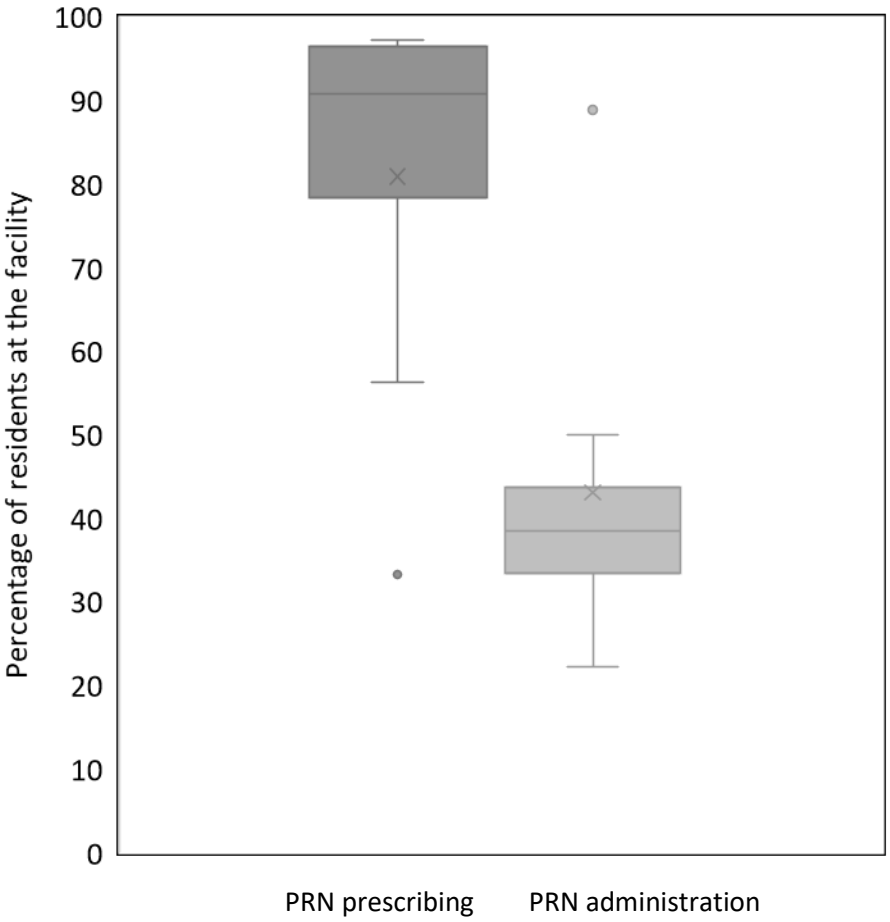
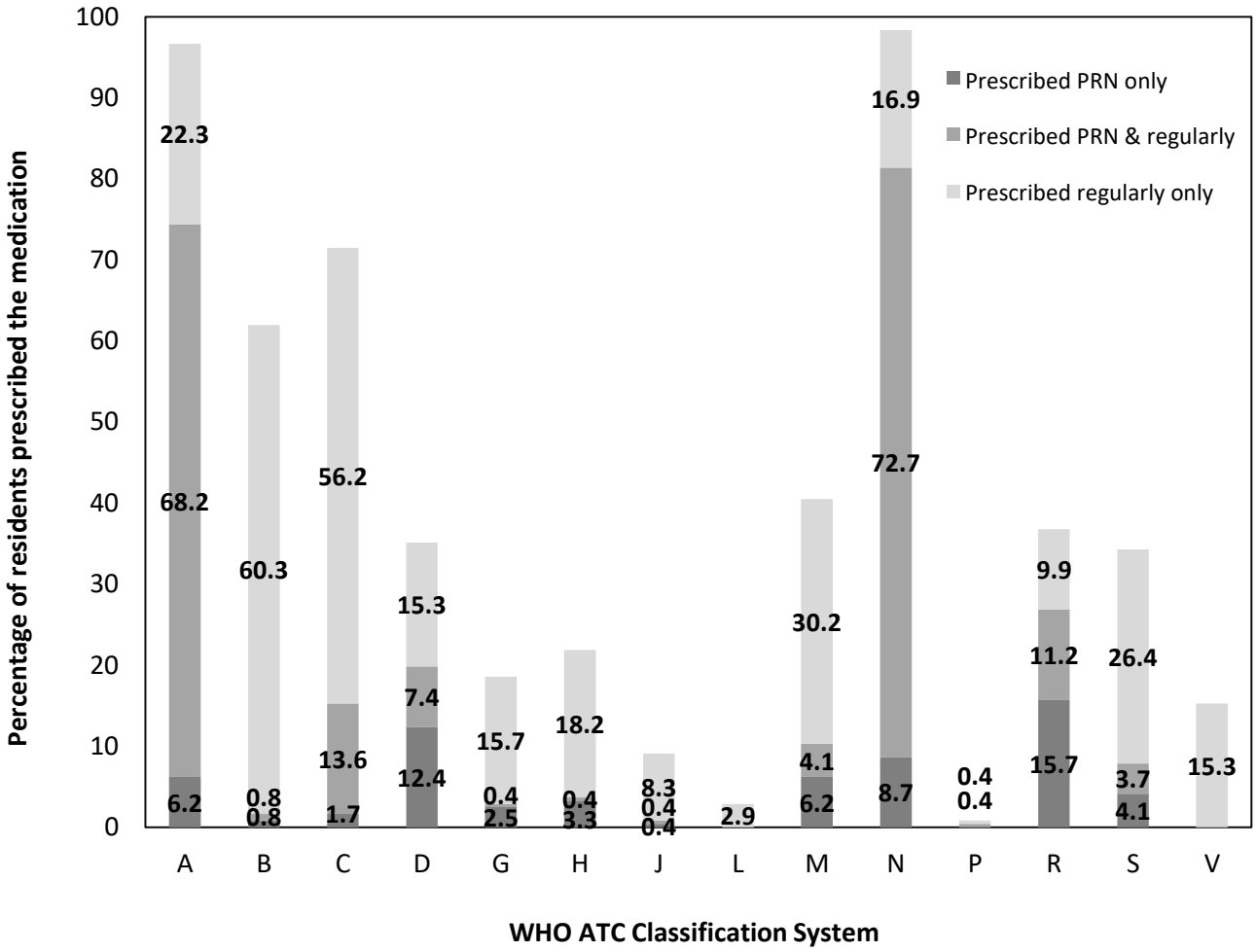


Figure 2. Prevalence of prescribing of *pro re nata* (PRN) and regular medications at study entry



WHO ATC classification codes

A = alimentary tract and metabolism; B = blood and blood forming organs; C = cardiovascular system, D = dermatologicals; G = genito-urinary system and sex hormones; H = systemic hormonal preparations, excluding sex hormones and insulins; J = anti-infectives for systemic use; L = antineoplastic and immunomodulating agents; M = musculoskeletal system; N = nervous system; P = antiparasitic products, insecticides and repellents; R = respiratory system; S = sensory organs; V = various.

Supplementary Table 1. Alimentary tract and metabolism and nervous system medications prescribed at baseline and 12-month follow up (n=162 residents)

Medication name/class	Medications prescribed regularly					Medications prescribed *pro re nata* (PRN)				
	Baseline (n, %)	Follow-up (n, %)	Medication started (n, %)	Medication stopped (n, %)	p-value*	Baseline (n, %)	Follow-up (n, %)	Medication started (n, %)	Medication stopped (n, %)	p-value*
Alimentary tract & metabolism	146 (90.1)	146 (90.1)	3 (1.9)	3 (1.9)	1.000	116 (71.6)	133 (82.1)	27 (16.7)	10 (6.2)	0.008
Laxatives	81 (50)	92 (56.8)	18 (11.1)	7 (4.3)	0.043	105 (64.8)	117 (72.2)	15 (9.3)	27 (16.7)	0.088
Nervous System	142 (87.7)	142 (87.7)	3 (1.9)	3 (1.9)	1.000	131 (80.9)	133 (82.1)	18 (11.1)	16 (9.9)	0.864
Opioids	44 (27.2)	48 (29.6)	11 (6.8)	7 (4.3)	0.481	54 (33.3)	58 (35.8)	21 (13.0)	17 (10.5)	0.627
Paracetamol	103 (63.6)	108 (66.7)	15 (9.3)	10 (6.2)	0.424	90 (55.6)	82 (50.6)	15 (9.3)	23 (14.2)	0.256
Antipsychotics	33 (20.4)	36 (22.2)	8 (5.0)	5 (3.1)	0.581	13 (8.0)	20 (12.3)	8 (4.9)	1 (0.6)	0.039
Anxiolytics	21 (13.0)	20 (12.3)	2 (1.2)	3 (1.9)	1.000	39 (24.1)	34 (21.0)	6 (3.7)	11 (6.8)	0.332
Hypnotics & sedatives	16 (9.9)	13 (8.0)	2 (1.2)	5 (3.1)	0.453	21 (13.0)	22 (13.6)	5 (3.1)	4 (2.5)	1.000

*McNemar's test