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RESEARCH ARTICLE

Initiation and continuation of antipsychotic medicines in older people following non-psychiatric hospital admission

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Abstract

Background Internationally, antipsychotics are frequently initiated during hospital admission for older patients and use often continues post-discharge without indication. We located no Australian studies on this topic. *Objective* to identify the hospital admissions (excluding psychosis) associated with antipsychotic initiation and continuation in older Australians. *Setting* Australian Government Department of Veterans' Affairs. *Method* Retrospective analysis of administrative claims data for people admitted to hospital from 1 January 2014 to 31 December 2014, aged ≥ 65 years, who were antipsychotic naïve. *Main outcome measure* number of admissions associated with antipsychotic initiation, and the major diagnosis groups for these admissions. Where antipsychotics were initiated, we determined the time to cessation of antipsychotics after discharge. *Results* There were 142,009 hospital admissions for 66,415 people with a median age of 86 years. 921 (0.65%) admissions were associated with antipsychotic initiation, most commonly where the primary diagnoses were for mental and behavioural disorders excluding psychosis (17.8%) and injuries (16%). Fourteen percent of antipsychotic initiations were for primary diagnoses of delirium or dementia. When secondary diagnoses were considered, 55% of antipsychotic initiations were associated with delirium, dementia or both. The median duration of use among people who used antipsychotics was 132 days, and 40% continued use until death or one year follow-up. *Conclusion* Initiation of antipsychotics during hospital admissions was not frequent in this Australian population. Amongst those who did initiate antipsychotics, for almost half no diagnosis corresponding with an approved indication for use was recorded and long-term use of up to one year was common.

Keywords Antipsychotic · Australia · Delirium · Dementia · Elderly · Hospital admission

Impacts on practice

- Initiation of antipsychotics during non-psychiatric hospital admissions was infrequent in our study population; however, amongst those who did start taking an antipsychotic, long-term use was common.
- Prescribers and pharmacists should ensure that antipsychotics are only supplied at hospital discharge if the benefits of use outweigh the risks, and plans for cessation should be clearly communicated to community health care providers.
- Particular care should be given to ensuring appropriate duration of antipsychotic use in people with dementia or delirium, conditions where antipsychotics should only be used short term if at all.

Introduction

Antipsychotics are indicated for the management of acute and chronic psychotic disorders and bipolar disorder [1]. Antipsychotics are also used to manage the behavioural and psychological symptoms of dementia (BPSD). In Australia, risperidone is the only antipsychotic approved for BPSD [1], and it is indicated for short term use of up to twelve weeks only [2]. Antipsychotics are commonly used to manage delirium in hospitalised patients, however, none have

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regulatory approval for this indication [3]. The benefits of using antipsychotics for delirium do not appear to outweigh the risks of harm [4].

International research suggests that antipsychotics are frequently initiated during hospital admission for older patients, and their use often continues post-discharge even when there is no clear indication for continued use. A retrospective cohort study of antipsychotic use in patients hospitalised for non-psychiatric diagnoses, which involved 2.6 million patients from 300 US hospitals, found that the risk of receiving an antipsychotic during the hospital admission was highest in those with delirium (adjusted relative risk (RR) 2.93, 95% confidence interval (CI) 2.88–2.98) and dementia (adjusted RR 2.78, 95% CI 2.72–2.83) [5]. A second study by the same authors found that of 17,775 adults admitted to a single hospital for non-psychiatric reasons between August 2012 and August 2013, 1537 people (9%) used antipsychotics during the admission, with just over half (n = 842) initiating the antipsychotic during the hospitalisation [5]. A quarter of patients who used antipsychotics in hospital (n = 222) were also discharged on antipsychotics [5]. Patients aged 75 years or over were more likely to use antipsychotics during the admission compared to those aged less than 65 (RR 1.4, 95% CI 1.2–1.7) but were less likely to be discharged on them (RR 0.6, 95% CI 0.4–0.7) [5]. Delirium (RR 4.8, 95% CI 4.2–5.7) and dementia (RR 2.1, 95% CI 1.7–2.6) were strong predictors of in-hospital use of antipsychotics but were not significantly associated with supply of antipsychotics at discharge [5]. Another retrospective analysis of 12,817 people aged 65 years or over who were admitted to a single US hospital between October 2012 and September 2013 for non-psychiatric conditions, found that 9% were initiated on antipsychotics during the admission [6]. Analysis of the medical records of a random sample of 300 of these patients found that delirium was the most common reason for antipsychotic use (86%), but a formal diagnosis using a validated delirium assessment tool was uncommon and was recorded in only 35% of these patients [6]. Dementia was also a common diagnosis (45% of patients). Nearly half of the patients were discharged from hospital on an antipsychotic [6].

Initiation of antipsychotics for reasons other than psychosis during hospital admission for older people is of concern because there is limited evidence for benefits of long term use of antipsychotics for non-psychiatric conditions and there is strong evidence for increased risk of serious adverse effects in older people, including hip fracture [7], pneumonia [7], stroke [8] and death [9]. We located no Australian studies on the rate of antipsychotic initiation and continuation associated with non-psychiatric hospital admission, so the extent of the problem in Australia is unknown. Therefore, the aim of this study was to identify the non-psychiatric hospital admissions associated with highest risk of antipsychotic initiation and continuation. We hypothesized that, like international research, there would be a higher risk of antipsychotic initiation and continuation following hospital admissions for delirium or dementia compared to other diagnoses.

Methods

Study design and data source

We conducted a retrospective analysis of Australian Government Department of Veterans' Affairs (DVA) administrative claims data. The DVA claims data contains details of all prescription medicines and hospitalisations provided to veterans for which DVA pay a subsidy. DVA maintains a client file, which includes data on gender, date of birth and date of death. Medicines are coded in the dataset according to the World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) classification [10] and the Schedule of Pharmaceutical Benefits item codes [11]. All medicines dispensed in the community and subsidised on the Pharmaceutical Benefits Scheme (PBS) or Repatriation Pharmaceutical Benefits Scheme (RPBS) are recorded in the dataset. Supply of all PBS or RPBS subsidised medicines dispensed during private hospital admissions are also recorded, while supply of PBS and RPBS subsidised medicines in public hospitals is only recorded for medicines dispensed at the time of discharge (excluding the states of New South Wales and the Australian Capital Territory, where discharge medicines supply is not subsidised under the PBS or RPBS). Hospitalisations are coded according to the WHO International Classification of Diseases—10th Edition, Australian Modification [12]. The median age of the DVA treatment population is 80 years.

Inclusion and exclusion criteria

We included people who were eligible for all health services subsidised by DVA, who were admitted to and discharged from hospital between 1 January 2014 and 31 December 2014, aged ≥ 65 years at the time of admission, and who were antipsychotic naïve at the time of admission (defined as no claim for dispensing of an antipsychotic medicine (ATC codes N05A excluding prochlorperazine and lithium) in the year prior to admission). People who were hospitalised for psychosis or other diagnoses where antipsychotics are indicated (ICD codes F20–F29, F323, F333, F39) during the year were excluded, as were people who died during their hospital admission (Fig. 1).

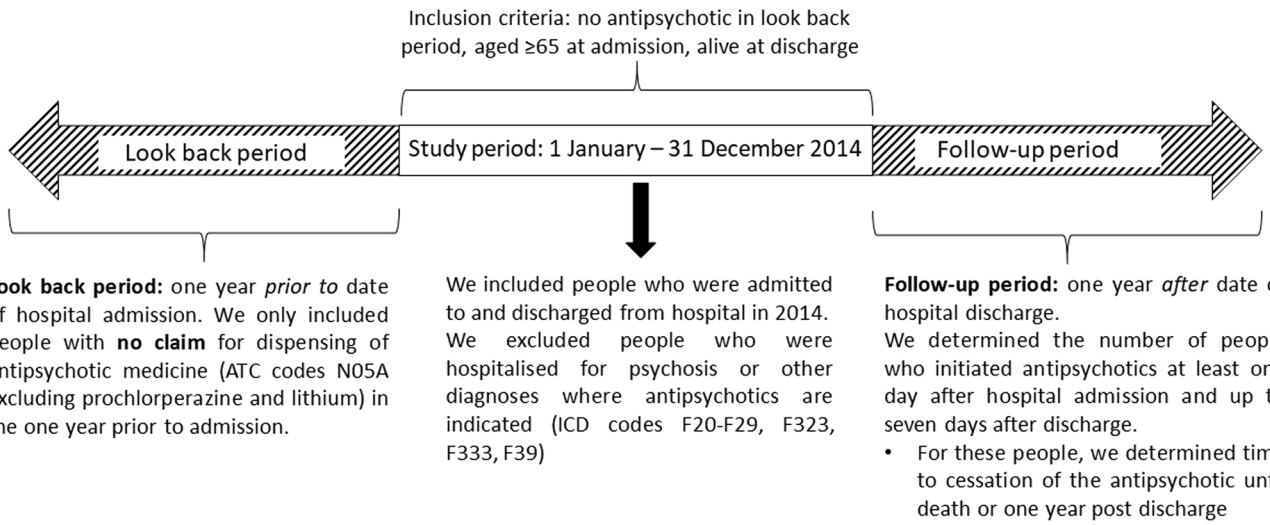

Fig. 1 Study design

Follow-up and outcomes

We determined the number of people who initiated antipsychotics between one day after hospital admission and seven days after discharge. If antipsychotics were initiated in this time frame, it was classified as being associated with the hospital admission. We chose this time frame because prior research in this population showed that the median time to visiting a pharmacy after a hospitalisation was approximately 7 days [13], and so this time frame would capture the first pharmacy visit after discharge for most patients. We determined the number of admissions associated with antipsychotic initiation. If an individual had multiple admissions during the study period, we included all admissions where the patient was antipsychotic naïve at the admission date. We determined the primary diagnoses for admissions associated with antipsychotic initiation by ICD chapter heading. In addition, we determined the number of admissions associated with antipsychotic initiation for the diagnoses of delirium (ICD code F05) or dementia (F00, F01, F02, F03, G30), or both, because prior studies found that these diagnoses were associated with in-hospital initiation of antipsychotics [5, 6]. We included secondary diagnoses in this analysis because these conditions may not be the primary reason for a hospitalisation but may complicate the admission or, as is the case with delirium, onset may occur during the hospital admission and therefore be recorded as a secondary diagnosis.

Statistical analysis

Where antipsychotic initiation was associated with a hospital admission, we determined the type of antipsychotic initiated and the time to cessation of antipsychotics after discharge (Fig. 1). We calculated the cumulative incidence function for time to cessation of antipsychotics after hospital admission. The dataset does not record prescription duration, so we calculated a duration estimate from the data based on the time within which 75% of individuals obtained a refill prescription for each antipsychotic [14]. Cessation was defined when there was no claim for dispensing of another antipsychotic within the period twice the time of the duration estimate from the last recorded dispensing, with the end date for antipsychotic use defined as the date of supply plus one duration estimate. Death was considered a competing event, analysis was performed using the Fine and Gray method [15]. Participants were followed from the date of antipsychotic initiation until cessation, date of death while still taking antipsychotic, or one year post-antipsychotic initiation, whichever came first.

We conducted two sensitivity analyses. In the first, we excluded public hospital admissions in New South Wales and the Australian Capital Territory, where medicines supply at the time of hospital discharge is not recorded in our dataset. For all other states, medicines dispensed at hospital discharge are recorded in our dataset, so antipsychotic dispensed at the time of hospital discharge is captured. Inpatient medicines supply is only recorded in our dataset for inpatients in private hospitals; inpatient supply of antipsychotics for people admitted to public hospitals is not recorded. Our method would capture ongoing supply of antipsychotics for patients discharged from public hospitals if the antipsychotic was dispensed at hospital discharge, but will have underestimated inpatient-only use of antipsychotics in public hospitals. Therefore, in our second sensitivity analysis, we limited the study population to people admitted to private hospitals, where all dispensings of medicines during hospital admission and at the time of discharge are captured.

Ethics approval to conduct the study was obtained from the University of South Australia Human Research Ethics committee and the Australian Government Department of Veterans' Affairs Human Research Ethics committee. All analyses were performed using SAS for windows, V9.1.3 SP4 (SAS institute, Cary, North Carolina, USA).

Results

There were 142,009 hospital admissions during the study period, for 66,415 individuals. Their median age was 86 years (interquartile range 76–90) and 33,291 (50.1%) were women. Antipsychotic initiation occurred during admission, or within seven days of discharge, for 921 (0.65%) admissions. The median age of people who initiated antipsychotic was 89 years (interquartile range 85–91) and 465 (50.5%) were women.

The most frequent primary diagnoses for admissions where antipsychotics were initiated were within the ICD chapter headings of mental and behavioural disorders excluding psychosis (17.8% of antipsychotic initiations), injuries (S00-T98, 16.1%) and diseases of the circulatory system (I00–I99, 11.3%) (Table 1). Seven percent of admissions where an antipsychotic was initiated had dementia recorded as the primary diagnosis, and 7% had delirium recorded as the primary diagnosis (Table 2). When considering both primary and secondary diagnoses, in 32% of admissions delirium was recorded, in 31% of admissions dementia was recorded and for 55% either delirium, dementia or both were recorded. The most frequently initiated antipsychotics were haloperidol and risperidone (Table 3).

Inpatient supply of antipsychotics for people admitted to public hospitals is not recorded in our dataset, so we were unable to determine how many people admitted to public hospitals initiated antipsychotics but ceased them prior to discharge. This information is recorded for private hospital admissions, and the antipsychotic was ceased prior to discharge in 12 of the 525 private hospital admissions where antipsychotic was initiated. This left 909 admissions in both public and private hospitals, where antipsychotic initiation was associated with the hospital admission (i.e. initiation occurred between one day after hospital admission and seven days after discharge). For these 909 antipsychotic initiations, the median duration of antipsychotic use was 132 days. Only 27% of people had ceased antipsychotic use within six weeks

Table 1 Characteristics of hospital admissions in the study (n = 142,009)

	Hospital admissions with no antipsychotic initiation (n = 141,088)	Hospital admissions with antipsychotic initiation (n = 921)
Public hospital admissions (%)	43,544 (30.9%)	396 (43.0%)
Private hospital admissions (%)	97,544 (69.1%)	525 (57.0%)
Number (%) of admissions by ICD chapter		
Certain Infectious and parasitic diseases (A00–B99)	1681 (1.2%)	18 (2.0%)
Neoplasms (C00–D48)	17,605 (12.5%)	97 (10.5%)
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (D50–D89)	4704 (3.3%)	11 (1.2%)
Endocrine, nutritional and metabolic diseases (E00–E90)	2573 (1.8%)	14 (1.5%)
Mental and behavioural disorders (F00–F99)*	7539 (5.3%)	164 (17.8%)
Diseases of the nervous system (G00–G99)	4790 (3.4%)	35 (3.8%)
Diseases of the eye and adnexa (H00–H59)	16,804 (11.9%)	3 (0.3%)
Diseases of the ear and mastoid process (H60–H95)	582 (0.4%)	0
Diseases of the circulatory system (I00–I99)	16,617 (11.8%)	104 (11.3%)
Diseases of the respiratory system (J00–J99)	8861 (6.3%)	86 (9.3%)
Diseases of the digestive system (K00–K93)	12,968 (9.2%)	42 (4.6%)
Diseases of the skin and subcutaneous tissue (L00–L99)	3408 (2.4%)	19 (2.1%)
Diseases of the musculoskeletal system and connective tissue (M00–M99)	10,426 (7.4%)	39 (4.2%)
Diseases of the genitourinary system (N00–N99)	6620 (4.7%)	51 (5.5%)
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (R00–R99)	14,015 (9.9%)	90 (9.8%)
Injury, poisoning and certain other consequences of external causes (S00–T98)	11,830 (8.4%)	148 (16.1%)

*Excluding diagnoses where antipsychotics are indicated for the management of the condition—Schizophrenia, schizotypal and delusional disorders (F20–F29); Severe depressive episode with psychotic symptoms (F323); Recurrent depressive disorder, current episode severe with psychotic symptoms (F333); Affective psychosis NOS (F39)

Table 2 Admissions with a diagnosis of delirium or dementia (or both) recorded

	Hospital admissions with no antipsychotic initiation (n = 141,088)	Hospital admissions with antipsychotic initiation (n = 921)
Admissions with		
Primary diagnosis of fracture	4435 (3.1%)	86 (9.3%)
Primary diagnosis of dementia	450 (0.3%)	60 (6.5%)
Primary diagnosis of delirium	588 (0.4%)	64 (6.9%)
Primary or secondary diagnosis of dementia	4412 (3.1%)	285 (30.9%)
Primary or secondary diagnosis of delirium	3558 (2.5%)	295 (32.0%)
Primary or secondary diagnosis of delirium or dementia or both	7385 (5.2%)	506 (54.9%)

Table 3 Types of antipsychotic initiated during admission (n = 921 admissions)

Haloperidol	397 (43.1%)
Risperidone	325 (35.3%)
Quetiapine	98 (10.6%)
Olanzapine	76 (8.3%)
Chlorpromazine	13 (1.4%)
Periciazine	9 (0.98%)
Other antipsychotics	3 (0.3%)

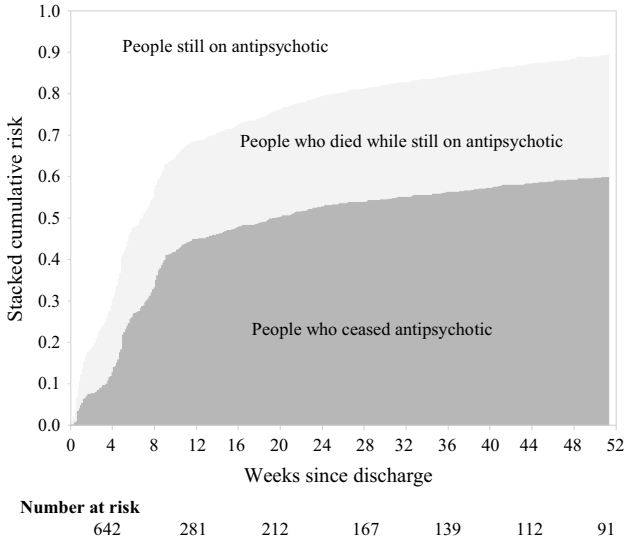

Fig. 2 Stacked cumulative incidence function for time to cessation of antipsychotics after hospital admission

of discharge; 40% of people continued to use the antipsychotic at the end of follow-up (12-months) or at the time they died (Fig. 2).

Both of our sensitivity analyses showed similar results to the overall analysis. After excluding public hospital admissions in NSW and ACT, where dispensing of medicines at discharge is not recorded in the dataset, we found that of 120,461 admissions, 756 (0.63%) were associated with antipsychotic initiation (supplementary table S1) and the types of antipsychotics initiated (table S2) were similar to the overall analysis. When we limited the analysis to private hospital admissions, 525 of 98,069 admissions (0.53%) were associated with antipsychotic initiation (table S3) and the types of antipsychotics initiated (table S4) were similar to the overall analysis. For both sensitivity analyses, the diagnoses for admissions most commonly associated with antipsychotic initiation (tables S1 and S3) were similar to the overall analysis.

Discussion

Our study shows that antipsychotic initiation during hospital admissions for primary diagnoses not related to psychosis is uncommon, but when it does occur, long-term antipsychotic use of up to one-year duration tends to follow. When we also considered secondary diagnoses for admissions associated with antipsychotic initiation, more than half had a primary or secondary diagnosis of delirium or dementia. This finding is of concern, because antipsychotics do not have regulatory approval for the management of delirium, and if used in the management of dementia, risperidone is the only antipsychotic approved for this indication, and short term use of up to 12-weeks is indicated. Results of our study, where the median duration of antipsychotic use was 132 days (approximately 19 weeks) and 40% of participants continued to use antipsychotic at the time of death or one-year post discharge, suggests that these guidelines were not followed for most patients.

The most frequently initiated antipsychotics in our study were haloperidol and risperidone. This reflects local medicines subsidy restrictions, where there are no restrictions for haloperidol, and risperidone is subsidised for the management of BPSD. In contrast, other antipsychotics like quetiapine and olanzapine are only subsidised in Australia for use in patients with schizophrenia, bipolar disorder or acute

mania; and people with hospital admissions for these diagnoses were excluded from our study. The frequency of use of haloperidol is also likely to reflect Australian practice for the management of in-hospital delirium. An Australian survey of hospital pharmacists found that, although haloperidol is not approved for use in the management of delirium, more than half of the pharmacists surveyed (53%) reported that haloperidol was the most common first line treatment for delirium in their hospital [16].

Although the absolute number of people who initiated antipsychotics in hospital admissions without psychiatric diagnoses in our study was low (921 people), the potential population impact is large. An Australian study estimated the number needed to harm associated with atypical antipsychotic use was 40 for hip fracture and 13 for pneumonia [7]. Applying these risk estimates to our study population, where 921 people initiated antipsychotics, indicates there may be 23 additional hip fractures and 71 additional cases of pneumonia for the patients in our study, that likely would not have occurred had they not used an antipsychotic. This is of particular concern because the antipsychotic initiations in our study were for admissions with no psychiatric diagnoses recorded, where there is limited evidence for any benefit associated with long-term use. If the rate of antipsychotic initiation in our study is applicable to the wider older Australian population the public health impacts would be significant. Future research should be conducted to determine the degree to which antipsychotic initiation is associated with non-psychiatric hospital admissions for the overall older Australian population.

The prevalence of antipsychotic initiation in our study was lower than international estimates. One US study which involved over 2.5 million adults admitted for non-psychiatric diagnoses found that antipsychotics were used in 6% of all admissions [5]. When limited to admissions for people aged 65–74 prevalence of use was 5%, and amongst people aged 75 or older, prevalence was 9% [5]. However, results of this study are not directly comparable to ours because in this study both incident and prevalent antipsychotic users were included. Other studies have assessed the frequency of antipsychotic continuation amongst people who initiate antipsychotics during hospital admission, and have reported continuation rates of 4% in general hospital populations [17] and 24% in people discharged from the intensive care unit [18]. We located no studies that assessed the duration of antipsychotic use post-discharge for antipsychotics initiated in non-psychiatric hospital admissions.

There are several limitations to our study. We excluded patients if they had been admitted to hospital with a primary or secondary diagnosis of schizophrenia or other conditions where long-term antipsychotic use is indicated. We did this to limit the likelihood that we identified appropriate initiation of antipsychotics. We cannot exclude the possibility that some admissions where antipsychotics were initiated were for appropriate indications but were coded for non-psychiatric diagnoses, or that ICD-10 codes relating to the management of psychiatric diagnoses were not coded for the admissions. We did not have access to discharge summaries for the patients in our study. It may be that some of the patients in our study who initiated antipsychotics had evidence based reasons for ongoing use documented at discharge, or that plans for cessation in the community were communicated to community health care providers.

Inpatient supply of medicines in public hospitals is not recorded in our dataset, so people who received an antipsychotic during public hospital admission, but discontinued use prior to discharge were not identified. Additionally we will have underestimated antipsychotic duration for initiation during public hospital admission, as time to cessation was measured from first dispensing post-discharge. Our sensitivity analysis, where we limited the analysis to private hospital admissions where inpatient dispensings of antipsychotics are recorded, found that prevalence of antipsychotic initiation was 0.53% in private hospitals (compared to 0.65% in the overall cohort, admitted to either public or private hospitals). This suggests that we are unlikely to have underestimated antipsychotic initiation in our analysis.

Conclusion

Initiation of antipsychotics during non-psychiatric hospital admissions was infrequent in our study population; however, amongst those who did initiate, long-term use of up to one-year duration was common. Slightly more than half of initiations were for admissions with a diagnosis of dementia or delirium, conditions where antipsychotics should only be used short term if at all. Prescribers and pharmacists should ensure that antipsychotics are only supplied at hospital discharge if the benefits of use outweigh the risks, and plans for cessation should be clearly communicated to community health care providers.

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Conflicts of interest The authors declare that they have no conflict of interest.

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