

# Use of High-Risk Psychotropic Medications and Delirium Assessment in Older Adults Undergoing Elective Surgery

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## Abstract

Several widely prescribed psychotropic medications are known to elevate the risk of postoperative delirium. In certain situations, temporarily reducing or withholding these medications before elective surgery could potentially lower this risk. However, the extent to which patients use these medications before planned surgical procedures remains unclear. This study aimed to assess the prevalence of opioid analgesics, antidepressants, gabapentinoids, and benzodiazepines used before elective surgery, to examine the frequency of delirium screening both pre- and postoperatively, and to determine the incidence of postoperative delirium among older patients taking high-risk medications. We performed a retrospective review of electronic medical records from four acute-care hospitals. Patients aged 65 years or older who underwent scheduled surgery within a two-week window were included. Data on demographics, surgical type and duration, anesthesia method, medications on admission, and 4AT delirium assessments were extracted from the records. The project was exempt from formal ethics approval under Central Adelaide Local Health Network (CALHN) Human Research Ethics Committee policy (Reference: CALHN19857), as it met the criteria for an audit, adhered to national ethical guidelines, and posed no foreseeable risk to patients. The analysis included 158 patients with a median age of 75 years. Before surgery, 41% were taking at least one medication linked to increased postoperative delirium risk: 21% were on antidepressants, 15% on opioid analgesics, 13% on benzodiazepines, and 6% on gabapentinoids. Preoperative delirium assessment with the 4AT tool was completed for 80% of participants, whereas 61% underwent at least one postoperative 4AT evaluation. A substantial proportion (41%) of older adults undergoing elective surgery were using medications associated with heightened postoperative delirium risk, yet delirium screening was not universally performed before or after surgery.

**Keywords:** Postoperative delirium, Delirium, Medicines, Elective surgery

## INTRODUCTION

Delirium is a complex clinical syndrome marked by acute confusion, impaired attention, disorganized thinking, and altered consciousness [1]. In Australia during 2021–2022, it ranked as the second most common hospital-acquired complication [2], affecting nearly 25,000 hospital separations [3], yet studies suggest that up to 40% of cases could be prevented [4]. Medications are a well-recognized, modifiable risk factor for postoperative delirium [5]. Specifically, preoperative exposure to beta blockers [6], benzodiazepines [5–7], opioid analgesics [6], anticholinergic drugs [6], antidepressants [5, 6], and gabapentinoids [7] has been associated with an elevated risk of developing delirium after surgery. For example, among patients aged 65 years or older undergoing hip or knee arthroplasty, treatment with sertraline was associated with one extra case of postoperative delirium per 43 patients (number needed to harm, NNH) [5]. Comparable NNH values were 40 for citalopram, 57 for mirtazapine, and 26 for nitrazepam [5]. The risk escalates with age: for patients over 85, the NNH for these medications is more than halved [5]. While some evidence has found no clear link between these medications and postoperative

delirium [8], the majority of research supports an increased risk with preoperative use.

Several psychotropic agents—including opioids, benzodiazepines, anticholinergics, gabapentinoids, and certain antidepressants—appear on lists of potentially inappropriate medicines for older adults [9, 10]. As a result, minimizing their use in the perioperative period is considered a prudent strategy. In many cases, these medications can be

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safely tapered or temporarily withheld before elective surgery, offering an opportunity to reduce the likelihood of postoperative delirium. Although interventions targeting the reduction of high-risk medicines before surgery have demonstrated effectiveness [11, 12], this approach is not routinely included in delirium prevention programs [13], and there is limited information on how often older patients actually use these medications before planned surgery.

Postoperative delirium is frequently underdiagnosed [14, 15]. One study revealed that only 30% of hospital records documented delirium for patients who experienced it [15]. This under-recognition is partly explained by the predominance of hypoactive delirium, which may account for up to 75% of cases [14] and often manifests as drowsiness or inactivity, potentially mimicking dementia or depression [16]. Clinical guidelines recommend early delirium assessment—within 24 hours of hospital admission or in preadmission clinics for elective surgery—for patients at elevated risk, including adults aged 65 years or older (or Aboriginal and Torres Strait Islander adults aged 45 years or older), individuals with pre-existing cognitive impairment, those with previous episodes of delirium, patients with severe or worsening illness, and those admitted with hip fractures [4]. Despite these recommendations, adherence is inconsistent; a baseline audit in an Australian hospital found that only 20% of high-risk patients underwent delirium screening on admission [17].

Reducing the incidence of postoperative delirium requires targeted interventions. Current prevention strategies, however, rarely focus on safely decreasing the use of high-risk psychotropic medications before planned surgery. To develop effective interventions, it is essential to understand how frequently older adults use these medications before surgery and how often they experience postoperative delirium. Accordingly, this study aimed to quantify the prevalence of high-risk medication use before elective surgery, evaluate the rates of pre- and postoperative delirium screening, and determine the incidence of postoperative delirium among older patients taking these medications.

## MATERIALS AND METHODS

### Study Design

A retrospective review of electronic medical records (EMRs) was conducted across four public acute-care hospitals within the Central and Northern Adelaide Local Health Networks in South Australia. Two of these hospitals were large tertiary referral centres, while the remaining two were smaller acute-care facilities, all situated in metropolitan Adelaide. Each site provides a variety of surgical services, including general surgery, gastroenterology, breast and endocrine surgery, vascular, orthopaedic, spinal, plastic, and urology procedures. A state-wide EMR system is in place, ensuring uniformity of records across all hospitals. Delirium assessments were conducted using the 4AT (4 ‘A’s Test) integrated into this EMR.

Patient records were retrieved for individuals aged 65 years or older who underwent planned surgery between 17 and 31 July 2023. Participants were included consecutively. Extracted data included patient age, sex, surgical procedure type, surgery duration, and type of anaesthesia. Medications at the time of admission were determined using the best possible medication history (BPMH), obtained by a pharmacist either in the preadmission clinic or upon hospital admission. The BPMH is a comprehensive inventory of current medications compiled from multiple sources, including a review of prior records (such as medication lists and previous admissions), patient or caregiver interviews to confirm actual medication use, and verification with community pharmacies, general practitioners, or the patient’s medication containers [18].

If a pharmacist-led BPMH was unavailable, medications documented by medical officers at admission were used. In the absence of either source, current medicines were identified via the national Australian electronic health record system, My Health Record. The total number of drugs in use at admission was calculated, including both regular and “as needed” (prn) medications. Specific attention was given to the use of opioid analgesics, benzodiazepines, gabapentinoids, and antidepressants at the time of admission, as these medications are known to increase the risk of postoperative delirium [5-7] and may, in some cases, be safely reduced before planned surgery [19].

Delirium evaluations recorded in the EMRs were based on the 4AT, a validated four-item tool designed to assess both delirium and cognitive impairment [20]. The 4AT examines alertness, cognition, attention, and acute changes or fluctuations in mental function. Scores range from 0 to 12, where a score of 4 or higher suggests delirium, 1–3 indicates cognitive impairment, and 0 implies that delirium or cognitive impairment is unlikely [21]. Interpretation of the 4AT should always be supplemented with clinical judgment. The tool demonstrates 82% sensitivity and 88% specificity for detecting delirium [20] and was selected because it is routinely employed across South Australian (SA) Health facilities [22]. Local protocols recommend completing the 4AT for all individuals aged over 65 as part of standard delirium screening upon hospital presentation—within 8 hours of arrival or within 2 hours if delirium symptoms are evident [22]. Reassessment is advised whenever patients exhibit new or changing cognitive symptoms or behaviors [22]. These local recommendations align with national delirium care standards issued by the Australian Commission on Safety and Quality in Health Care, which advocate screening high-risk individuals, including those aged 65 and above, using validated tools such as the 4AT within 24 hours of admission [4].

Descriptive statistics were used to summarise the data. Specifically, we calculated the proportion of participants taking at least one medication known to increase the risk of postoperative delirium at admission, as well as the median

number of such medicines per patient (interquartile range [IQR]). The number of participants with a 4AT assessment performed preoperatively and postoperatively was recorded, along with those whose 4AT scores indicated delirium (i.e., scores  $\geq 4$ ). In cases where multiple postoperative 4AT assessments were completed, the highest score was reported. Following Australian Bureau of Statistics guidance, aggregate data with counts  $< 5$  were not included in tables to prevent potential identification of individuals [23].

All statistical analyses were conducted using SPSS Statistics (IBM Corp., Armonk, NY, USA).

## RESULTS AND DISCUSSION

The study included 158 participants, with a median age of 75 years; 40% were female. Surgical admissions were primarily for urology (18%), orthopaedics (11%), and colorectal procedures (11%) (**Table 1**). The median surgery duration was 2 hours, and 71% of participants received a general anaesthetic. A pharmacist obtained the best possible medication history (BPMH) for 62% of participants, while 27% had their medication history documented by a medical officer. For 10% of participants, no medication history was recorded at admission (**Table 1**). Among those with available medication histories, the median number of medicines in use at admission was seven (**Table 1**).

**Table 1. Participant characteristics (n = 158)**

Characteristic	Value
Median age (years, IQR)	75 (70–80)
Gender, n (%)	
Female	63 (40%)
Male	95 (60%)
Type of surgery, n (%) <sup>a</sup>	
Urology	28 (18%)
Orthopaedic	18 (11%)
Colorectal	17 (11%)
Gastroenterology	14 (9%)
Plastic	12 (8%)
Vascular	13 (8%)
Median surgery duration (minutes, IQR) <sup>b</sup>	119 (72–190)
Anaesthesia type, n (%)	
General	112 (71%)
General + regional	3 (2%)
Regional	11 (7%)
Sedation	24 (15%)
Local	6 (4%)
Not reported	2 (1%)
Medication history source at admission, n (%)	
Pharmacist BPMH	98 (62%)
Medical officer	43 (27%)
My health record or prior admission	10 (6%)
No medication history available	7 (4%)
Median number of medicines at admission (IQR)	7 (4–11)

Notes: IQR = interquartile range; <sup>a</sup> Table shows the most frequently recorded surgical procedures; <sup>b</sup> Surgery duration was documented for 154 participants.

Of the 151 participants for whom a medication list was available at admission, 43% were taking at least one medicine linked to an increased risk of postoperative delirium before their scheduled surgery (**Table 2**). Specifically, 22% were on an antidepressant, 16% were using an opioid analgesic, 14% were taking a benzodiazepine, and 6% were prescribed a gabapentinoid at the time of admission (**Table 2**).

**Table 2. Admission use of medications linked to high postoperative delirium risk (n = 151)<sup>a</sup>**

Medication use	N (%)
Participants taking $\geq 1$ high-risk medicine	65 (43%)
Medication types, n (%)	
Opioid analgesics	24 (16%)
Antidepressants	33 (22%)
Gabapentinoids	9 (6%)
Benzodiazepines	21 (14%)
Median number of high-risk medicine types (IQR) <sup>b</sup>	1 (1–3)

Notes: <sup>a</sup> Although 158 participants were included in the study, 7 did not have a medication list at admission; only the 151 participants with available medication histories are included here; <sup>b</sup> Calculated for participants taking at least one type of high-risk medication.

Pre-surgery 4AT assessments were completed for 80% of participants. Among those assessed, 107 individuals (84%) had a score of 0, indicating no signs of delirium or cognitive impairment before surgery. Following surgery, 61% of participants underwent at least one postoperative 4AT evaluation, with 84 of them (87%) scoring 0. Postoperative delirium was infrequent in this group, with fewer than five participants registering a 4AT score of 4 or higher (**Table 3**). Of the 20 participants who scored 1 or above on the preoperative 4AT, 15 (75%) received a postoperative assessment, and 11 of these had a postoperative score of at least 1, suggesting persistent cognitive changes.

**Table 3. Delirium assessment of participants pre- and post-surgery**

Measure	N (%)
Participants with a preoperative 4AT assessment	127 (80%)
Participants with a postoperative 4AT assessment	97 (61%)
Preoperative 4AT scores (n = 127)	
Score = 0 (no delirium/cognitive impairment)	107 (84%)
Score 1–3 or $\geq 4$ <sup>a</sup>	20 (16%)
Postoperative 4AT scores (n = 97)	
Score = 0	84 (87%)
Score 1–3 or $\geq 4$ <sup>a</sup>	13 (13%)

Notes: <sup>a</sup> Scores of 1–3 suggest likely cognitive impairment, while scores  $\geq 4$  indicate probable delirium; pre- and post-surgery categories were combined because fewer than five participants had 4AT scores  $\geq 4$ .

In our study, 41% of older adults scheduled for planned surgery were taking an opioid analgesic, antidepressant, benzodiazepine, or gabapentinoid before surgery. These medications are known to increase the risk of postoperative delirium, highlighting an opportunity to safely reduce their use before planned procedures to mitigate this risk. The proportion of patients using these medications in our cohort closely aligns with previously reported figures. For instance, a matched case-control study using administrative claims data from the Australian Government Department of Veterans' Affairs, which included individuals aged 65 years and older undergoing hip or knee surgery, found that 13% of cases and controls were using opioid analgesics at the time of surgery (compared to 15% in our study), 22% were on antidepressants (versus 21% in our research), and 14% were using benzodiazepines (versus 13% in our study) [5]. However, that study was limited in that it could not confirm actual medication use at admission, as it only tracked dispensing records near the admission date, and included patients undergoing both planned and emergency surgery. Our findings contribute additional insight by identifying the medications patients were actively using at admission for planned surgery.

Delirium screening is recommended for all individuals aged 65 years or older within 24 hours of hospital admission [4, 22]. In our cohort, 80% of participants underwent a 4AT assessment before surgery, in accordance with these recommendations. While preoperative 4AT screening identified cognitive impairment in only 20 patients, nearly all of these patients ( $n = 15$ , 75%) received follow-up 4AT testing postoperatively. The 2021 Delirium Clinical Care Standard recommends that patients with one or more delirium risk factors undergo screening within 24 hours of admission, and those with possible cognitive impairment should be subsequently assessed for delirium [4]. Our results suggest that this guidance was mainly adhered to for patients undergoing planned surgery at the study sites during the study period.

Instances of delirium, as indicated by 4AT scores, were uncommon in our study. Fewer than 5 of the 97 patients who received a postoperative 4AT assessment had scores of four or higher, suggestive of delirium. Similarly, fewer than 5 of the 127 patients assessed preoperatively had 4AT scores of four or above. To protect participant anonymity, exact numbers in these categories were not reported [23]. Comparing our findings with previous research suggests that delirium prevalence may have been underestimated. For example, a prospective study of non-surgical patients aged seventy years and older admitted to 4 Australian hospitals reported delirium in 10% of 493 patients at admission, with an additional 8% developing delirium during hospitalization [24]. That study utilized the Confusion Assessment Method to detect delirium [24]. A systematic review and meta-analysis of international studies reported pooled postoperative delirium rates in older adults ( $\geq 65$  years) as 18% for planned orthopaedic surgery, 14% for planned

vascular or colorectal surgery, 11% for planned spinal surgery, 32% for planned cardiac surgery, and 10% for planned urological surgery [25]. Although screening methods varied across studies, the Confusion Assessment Method was the most commonly employed tool for identifying delirium [25].

Although surgeries included in our study were commonly performed, the observed rate of postoperative delirium was notably lower than expected. One possible explanation for this difference is our study's inclusion criteria. We focused exclusively on patients undergoing planned procedures, excluding those whose surgeries were postponed or cancelled due to preoperative delirium. While dementia is a strong predictor of postoperative delirium, only 16% of participants had a preoperative 4AT score suggestive of cognitive impairment. In contrast, previous systematic reviews and meta-analyses report much higher rates of cognitive impairment: over 50% among patients undergoing vascular surgery [26], up to 37% in planned orthopaedic surgery, and 26% in cardiac surgery [27]. This discrepancy indicates that either the prevalence of dementia was lower in our study population, or cognitive impairment was underdetected and underreported. These findings suggest that relying on retrospective hospital electronic records and routinely collected 4AT scores likely underestimates the true incidence of postoperative delirium, highlighting the need for prospective investigations to validate this hypothesis.

Regarding medication history, 62% of participants had a Best Possible Medication History (BPMH) recorded by a pharmacist upon admission, with an additional 27% documented by a medical officer. Despite guidelines recommending that all patients have a BPMH completed promptly upon hospital admission [28, 29], studies internationally show that this is often not achieved for patients undergoing planned surgery. For instance, a study in the United States reported that, before interventions aimed at improving pre-surgical BPMH completion, only 77% of patients had a pharmacist-led medication history before surgery. The authors noted that histories were frequently obtained "just moments before surgery, which may be rushed, incomplete, or missed entirely" [30].

Data on BPMH completion in Australian preoperative populations are limited. A study conducted in 2007–2008 found that 81% of patients randomized to receive a pre-surgical pharmacist review in a preadmission clinic had their medications reconciled before surgery, compared with 75% in the standard care group [31]. Pharmacists were only available on days when patients undergoing orthopaedic, colorectal, or vascular procedures attended, reflecting a focus on those considered most likely to benefit from review. A 2023 study from Western Australia reported that pharmacists in a gynaecological oncology preadmission clinic reviewed 26% of patients, two-thirds of whom were classified as 'high-risk,' and that 93% of high-risk patients attending the clinic received a pharmacist review [32]. Together, these findings



suggest that pharmacists tend to prioritize BPMH documentation for patients at higher risk. It is possible that, in our study, BPMHs were similarly more likely to be recorded for patients deemed at most significant risk due to staffing or resource constraints. However, this possibility was not formally assessed in our study, and further research is needed to explore the factors influencing selective BPMH completion.

Like any research study, this investigation has several limitations that should be considered when interpreting the findings. It is possible that some participants had a BPMH or 4AT assessment that was performed but not recorded in the electronic medical record (EMR). Additionally, because the EMR allows previous 4AT scores to be copied forward, there is a risk that some scores may not accurately reflect the patient's current cognitive state. This could partly explain the low rate of delirium observed in our cohort.

Our study focused on patients who underwent planned surgery. Individuals who had delirium detected during baseline screening and subsequently had their surgery postponed or cancelled would not have been included, suggesting that baseline delirium may have been underestimated. Furthermore, only 61% of participants had a postoperative 4AT assessment, meaning that some cases of delirium could have gone undetected. It should be noted, however, that local protocols recommend repeating the 4AT only if there are changes in cognition or behaviour [22], so the lower rate of postoperative assessments may reflect that few patients exhibited new or altered cognitive symptoms. Prospective data collection would help overcome these limitations and provide a more accurate picture of delirium prevalence.

This study did not investigate non-pharmacological contributors to postoperative delirium. The combined influence of medications, existing comorbidities, and other risk factors, such as frailty, warrants further investigation. We specifically examined the use of opioid analgesics, antidepressants, gabapentinoids, and benzodiazepines due to their known association with postoperative delirium. However, other medications may also contribute to delirium risk, and future research should aim to capture a broader range of drugs.

Although delirium screening is recommended for Aboriginal and Torres Strait Islander patients aged 45 years and older, so few individuals met this criterion at our study sites that reporting results could risk identification; consequently, these data were not included.

## CONCLUSION

This study highlights that 41% of older adults undergoing planned surgery were taking at least one high-risk medication, including benzodiazepines, antidepressants, opioid analgesics, or gabapentinoids, at the time of surgery.

Delirium screening was conducted for 80% of patients on admission and 61% postoperatively. These findings underscore the need for strategies to prevent postoperative delirium, including careful review and potential reduction of high-risk medication use before planned surgery.

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