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The prevalence of antipsychotic polypharmacy and its associations with violent behaviors among forensic psychiatry patients

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Abstract

Background Effective control of psychotic symptoms and behavioral problems is crucial in forensic psychiatric settings to enhance recovery and manage different risk concerns. While antipsychotic polypharmacy is commonly employed to ensure symptom control and risk mitigation, there is limited research on its burden and relationship with violent and aggressive behaviors in forensic psychiatric populations.

Objectives This study aims to examine the prevalence of antipsychotic polypharmacy among forensic psychiatry patients in Ontario and assess its relationship with recent incidents of aggression and violence.

Methods We conducted a retrospective analysis using a database prepared from data captured in annual reports submitted to the Ontario Review Board by 12 forensic programs in Canada. We utilized statistical analyses based on negative binomial regression to evaluate associations between antipsychotic polypharmacy and incidences of violence.

Results Among 1,104 patients in the databases, 37.8% ($n=417$) were on antipsychotic polypharmacy. The most frequent combination was with Olanzapine or Quetiapine. Antipsychotic polypharmacy was more likely among individuals with increased incidents of physical violence to objects (adjusted incidence rate ratio [IRR]: 1.69; 95% Confidence Interval [CI]: 1.07–2.68; $p=0.025$), self-harm (IRR: 3.30; 95% CI: 1.29–8.44; $p=0.013$), and sexually inappropriate behavior (IRR: 2.43; 95% CI: 1.35–4.36; $p=0.003$) and aggression (IRR: 1.57; 95% CI = 1.10–2.27; $p=0.014$).

Conclusions Antipsychotic polypharmacy is prevalent among forensic psychiatry patients, and more likely among those with violent and aggressive behaviors. These findings underscore the need for innovative approaches and further research to inform clinical guidelines, thereby improving patient safety and treatment efficacy.

Clinical trial number Not applicable.

Keywords Antipsychotic polypharmacy, Forensic psychiatry, Violence, Self-harm

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Introduction

Forensic mental health systems are designed to care for individuals with mental disorders who commit violent offences and other crimes, aiming to promote their recovery, manage risk, and enhance public safety [1]. To achieve this, biopsychosocial treatment approaches (involving pharmacological and non-pharmacological treatments) are implemented to manage forensic patients, although psycho-pharmacological treatments are predominant [2–7]. Nonetheless, the care of patients in forensic psychiatry (the majority of whom are diagnosed with psychotic illnesses) is especially challenging, particularly as treatment adherence, behavioural problems, aggression, commodities, and violence often present additional complexities [8–10].

Antipsychotic medications remain a crucial treatment in forensic psychiatry, with clinical guidelines consistently recommending an evidence-based approach to psychotropic drug use. Monotherapy or using fewer medications is preferred when appropriate to minimise side effects, prevent drug interactions, improve adherence, and reduce pill burden [5, 11]. However, many patients do not achieve adequate symptom control or recovery with a single antipsychotic, even after trials of sufficient dose and duration [12–15]. This treatment resistance poses a significant clinical challenge, particularly in forensic psychiatry settings, often prompting clinicians to consider alternatives such as clozapine therapy [16–18]or, in some cases, antipsychotic polypharmacy [12–14, 19].

Antipsychotic polypharmacy is relatively common worldwide, especially among people with treatment-resistant conditions [12–20]. Contributing factors to antipsychotic polypharmacy include partial or non-response to monotherapy, inherited prescriptions from previous providers, concerns about relapse when switching treatments, and high rates of medication non-adherence [12, 21–24]. In such situations, clinicians may employ a combination of oral and long-acting injectable formulations to enhance adherence [25, 26]. Proponents of polypharmacy argue that different antipsychotics can have varying effects on receptors and pharmacodynamics, which could theoretically help address a wider range of symptoms [21]. For example, one drug may be more effective for positive symptoms (such as hallucinations, delusions, and disorganized behavior) [5, 11, 12]. At the same time, another may provide greater relief for negative symptoms like reduced motivation and social withdrawal [5, 11, 12]. However, it is important to emphasize that such potential benefits and the rationale for antipsychotic polypharmacy are largely based on theoretical reasoning and anecdotal or case-level clinical observations, with limited direct evidence from controlled studies [27].

Epidemiological data indicate that antipsychotic polypharmacy is prevalent across diverse populations. A meta-analysis of the burden of antipsychotic polypharmacy involving more than 4.4 million individuals reported a global prevalence of 24.8%, with the highest rates observed among patients with schizophrenia spectrum disorders (33.2%) and in Africa (38.6%) [12]. In forensic psychiatry, prevalence estimates are even higher, ranging from 35% in Greenland to nearly 55% in British Columbia, Canada [28–31]. While some studies suggest no major differences between forensic and general psychiatry patients [32], antipsychotic polypharmacy appears particularly entrenched in forensic settings. This is often attributed to complex clinical presentations, long inpatient stays, stronger indications for intensive symptom management, and the need to manage aggression and violent behavior [20, 28, 29]. Also, trial of a combination of antipsychotics may be employed when patients have active psychotic symptoms, aggression and violent behaviours for several reasons. First, a single medication may not adequately address the multifaceted nature of aggression in certain patients due to variability in responses to medications [20, 33, 34]. For instance, combining agents with distinct mechanisms of action can help target the underlying causes of aggression, which may stem from active symptoms of various psychiatric conditions such as schizophrenia or bipolar disorder [20]. Additionally, a combination of multiple antipsychotics at lower doses may help mitigate side effects that arise from treatment with high doses of a single medication, allowing for a more balanced and tolerable treatment approach [35]. While clozapine has been shown to lower aggression levels in treatment-resistant populations [16, 17, 36], its overall effectiveness may be improved when paired with other pharmacological agents that address concurrent mood or anxiety symptoms [5, 11]. Therefore, the use of antipsychotic polypharmacy may lead to improved management of symptoms and better control of aggressive behaviours, resulting in better patient outcomes and enhanced overall well-being. While antipsychotic polypharmacy strategies (and sometimes those involving clozapine) are sometimes pursued, evidence supporting improved outcomes is limited [5, 11, 35]. Importantly, antipsychotic polypharmacy carries well-documented risks, including metabolic syndrome, extrapyramidal symptoms, and worsening mood or agitation, some of which may paradoxically increase self-harm risk [37–39]; and even more crucial is that the potential effects of antipsychotic polypharmacy are not well established in controlled studies and existing research should be interpreted with caution.

Despite its widespread use, little is known about how antipsychotic polypharmacy is applied in forensic psychiatry in Ontario, particularly in relation to patterns of

prescribing and its association with aggressive or violent behaviours. This study, therefore, sought to provide empirical data on two key questions: (1) What is the prevalence of antipsychotic polypharmacy among forensic psychiatry patients in Ontario? and (2) What patient characteristics, including recent incidents of aggression or violence, are associated with its use? By focusing on these specific aims, the study offers context-specific insights that can inform prescribing practices, highlight gaps for future research, and contribute to evidence-based discussions about the practice of polypharmacy in forensic psychiatry.

Methods

Study design and setting

This retrospective study utilized the Ontario Review Board (ORB) database that captured information on variables from the annual reports prepared on patients within the 12 forensic psychiatric programs in Ontario, Canada. The reports contain details on patients' courses in the forensic psychiatric program, risk assessment, treatment, and other relevant psycho-legal information for the 2014/15 reporting year. These reports are compiled by healthcare professionals specialized in forensic psychiatry, including psychiatrists, psychologists, and allied healthcare providers. Each report encompasses comprehensive information about an individual's experiences within the forensic system, particularly noting their treatment and any violent behaviors toward themselves, others, or objects. While these reports share a consistent format, their lengths may vary significantly, reflecting the individual patient's experiences throughout the year. Significant events relating to the patients are documented in detail, with each year's progress integrated into the patient's history. The psychiatrist responsible for the patient reviews the report, ensuring its accuracy and taking full responsibility for the information when presenting it to the ORB. Reports are formally authorized by both the hospital administrators and the psychiatrist before submission.

Data collection

Research assistants with specialized training and considerable experience in forensic psychiatry meticulously extracted data from ORB hospital reports using a standardized coding form. Training was provided to them by an interdisciplinary team of experts, including psychiatrists, clinical psychologists, and forensic psychiatry researchers. To ensure accuracy and reliability, the coding process was conducted in pairs, with teams reaching a consensus on each patient after detailed discussions. Any uncertainties were resolved by the principal investigator, GAC, to maintain data integrity. The meticulously collected data were then systematically entered into SPSS for comprehensive cleaning and then exported to Stata version 17 for statistical analysis. For further information about this dataset, refer to related publications [40–48].

Operational definitions

Antipsychotic polypharmacy Defined as the concurrent prescription of more than one antipsychotic drug. Patients were coded as receiving polypharmacy if two or more antipsychotics were prescribed at the point of submitting the report. We did not capture "as required" (PRN) medications.

Aggression and Violent Behaviours For the current study, violent and aggressive incidents documented in ORB reports during the reporting year were coded into five categories: (1) physical harm to others, (2) self-injury, (3) sexual violence, (4) property damage, and (5) verbal aggression.

Eligibility

In the current analysis, we included individuals who had data on recent violent and/or aggressive behaviors. We excluded individuals who were not on any antipsychotic medication. We also excluded patients whose reports contained no information on violent or aggressive behavior for that year.

Study variables

The study examined the incidents of violence/aggression behaviors as the independent variables during the reporting year, with polypharmacy as the dependent variable. Co-variables were chosen based on previous research and discussions with forensic psychiatry experts specializing in violence and risk management. These co-variables included age, gender, clinical status (outpatient vs. inpatient), history of substance abuse, length of hospital stay, primary psychiatric diagnosis, Ontario Board Review Status (ORB) status (Not Criminally Responsible due to mental illness (NCR) vs. Unfit to Stand Trial (UST)), type of index offense (violent, sexual, or non-violent), number of prior violent crimes (derived from each patient's cumulative ORB record, which compiles information from all previous annual reports. For this study, "previous violence" was defined as any documented incident of aggression or violence occurring before the 2014/15 reporting year, and any history of violent or aggressive incidents within the forensic system before the reporting year. For individuals with more than one violent offence, these were accounted for under the total number of offences. On the other hand, total recent incidents were the summation of incidents of harm within the reporting year, encompassing all the aforementioned individual violent/aggressive behaviours.

Data analysis

The analysis plan was structured to understand the study objective comprehensively. We utilized Stata version 17 for all statistical operations. First, we conducted descriptive statistics to outline the individuals' demographic and clinical characteristics. These statistics specifically included detailed calculations of frequencies and percentages for categorical variables alongside means and standard deviations for continuous variables. Next, we calculated prevalence rates for polypharmacy. A description of the combinations of antipsychotic medications utilized complemented this. We applied appropriate statistical tests to explore the potential associations between polypharmacy and the study variables. Specifically, chi-square tests were used for categorical variables to evaluate independence, and student-independent t-tests were used for continuous variables to compare means between groups. Lastly, we performed five separate negative binomial regression analyses to examine the relationships between incidences of the various types of recent aggressive and violent behavior and polypharmacy. Recognizing the complexity of these relationships, we controlled all the study co-variates in the different models. We considered a 95% confidence interval and p-value of less than 0.05 for all these analyses.

Results

Characteristics of the selected patients

The final sample consisted of 1,104 individuals with documented recent histories of violence or aggression, following the exclusion of 26 cases with no information reported on such behaviors in their ORB reports. Most participants were male (85%, $n = 939$), and the majority were found NCR (92.5%, $n = 1021$). Furthermore, 85.4% ($n = 943$) had a diagnosis of a psychotic spectrum disorder.

Classification of antipsychotic medications identified

In total, 23 distinct antipsychotic agents were identified in the dataset, comprising both oral and parenteral formulations, including depot preparations. First-generation antipsychotics (FGAs) accounted for 12 drugs, spanning the phenothiazines, thioxanthenes, the butyrophenone haloperidol, and loxapine. Second-generation antipsychotics (SGAs) comprised 11 drugs. See Supplementary Table 1.

Prevalence of antipsychotic polypharmacy

Approximately 37.8% ($n = 417$) of the individuals were on more than one antipsychotic medication. See Table 1. Of those on polypharmacy, 332 were on two antipsychotics, while 85 were on three antipsychotics. Among those two antipsychotics, the most frequent combination was Olanzapine and Quetiapine ($n = 22$), followed by Olanzapine and Paliperidone decanoate ($n = 19$) and Quetiapine and Risperidone ($n = 19$). Among those on three antipsychotics, the most frequent combination was Clozapine, Olanzapine, and Zuclopenthixol decanoate ($n = 5$). Forty-three of the combinations involved the use of a non-long-acting antipsychotic and a long-acting antipsychotic medication. However, five individuals were on a combination of two long-acting antipsychotics. See Supplementary Table 2.

Among the 332 patients prescribed two-drug antipsychotic regimens, the majority were on two SGAs ($n = 185$, 55.7%). A substantial proportion ($n = 132$, 39.8%) prescribed a combination of one FGA and one SGA, while only a small minority ($n = 15$, 4.5%) were on two FGAs. Similarly, among the 85 patients prescribed three-drug regimens, the most common pattern was one FGA with two SGAs, observed in 39 cases (45.9%). This was followed closely by regimens consisting of three SGAs ($n = 34$, 40.0%). Less frequent were combinations of two FGAs with one SGA ($n = 9$, 10.6%) and those involving three FGAs alone ($n = 3$, 3.5%).

Distribution of antipsychotic polypharmacy across study variables

Table 1 compares the distribution of study variables between patients with and without antipsychotic polypharmacy. A statistically significant proportion of patients with antipsychotic polypharmacy were found among inpatients (59.7%) compared to outpatients (45.4%; $p < 0.001$). Those with antipsychotic polypharmacy also exhibited a higher prevalence of substance use (76.2% vs. 67.8%; $p = 0.003$). Furthermore, a history of violent charges was notably higher in the antipsychotic polypharmacy group (mean: 8; SD: 23.3) versus the non-polypharmacy group (mean: 4; SD: 14.7; $p = 0.001$). Participants with antipsychotic polypharmacy were more likely to have a history of harm to others before the reporting year (58.7% vs. 48.4%; $p = 0.001$), harm to objects (39.6% vs. 26.1%; $p < 0.001$), and verbal aggression (72.2% vs. 60.6%; $p < 0.001$). Additionally, a higher percentage of individuals with antipsychotic polypharmacy had engaged in harming themselves (18.8% vs. 13.4%; $p = 0.018$) and sexual violence (33.5% vs. 26.9%; $p = 0.021$) before the reporting year.

Distribution of antipsychotic polypharmacy across recent violence/aggression incidents

Individuals involved in recent incidents of violent or aggressive behavior were statistically more likely to be prescribed antipsychotic polypharmacy. The most significant difference was observed in cases of verbal aggression, followed by incidents of physical self-harm. The least difference was noted in individuals involved in sexual abuse. For further details, refer to Table 2.

Table 1 Participant characteristics distribution prevalence of polypharmacy

Variable	All participants	Antipsychotic Polypharmacy		z/t/ χ^2(*p* value)
		No 687 (62.2)	Yes 417 (37.8)	
Age [*mean (SD)]*	42 (13.0)	42 (13.2)	42 (12.6)	1.04 (0.296)
Sex				
Male	939 (85.0)	590 (85.9)	349 (83.7)	2.44 (0.295)
Female	163 (14.8)	95 (13.8)	68 (16.3)	
Transgender	2 (0.2)	1 (0.3)		
Clinical status				
Outpatient	543 (49.2)	375 (54.6)	168 (40.3)	**21.22 (< 0.001)**
Inpatient	561 (50.8)	312 (45.4)	249 (59.7)	
Substance use history (*n* = 1.78)				
No	313 (29.0)	216 (32.2)	97 (23.8)	**8.59 (0.003)**
Yes	765 (71.0)	455 (67.8)	310 (76.2)	
Length in forensic psychiatry system/yrs [median (IQR)]	5 (2–9)	5 (2–9)	5 (2–10)	-1.43 (0.152)
ORB status				
UST	83 (7.5)	55 (8.0)	28 (6.7)	0.62 (0.430)
NCR	1021 (92.5)	632 (92.0)	389 (93.3)	
Previous violent charges [mean (SD)]	6 (18.5)	4 (14.7)	8 (23.3)	**-3.40 (0.001)**
Diagnosis				
Psychotic disorder	943 (85.4)	575 (83.7)	368 (88.2)	5.61 (0.230)
Mood disorders	85 (7.7)	62 (9.0)	23 (5.5)	
Neurodevelopmental Disorder (NDD)	34 (3.1)	21 (3.1)	13 (3.1)	
Neurocognitive Disorder (NCD)	16 (1.4)	11 (1.6)	5 (1.2)	
Others	26 (2.4)	18 (2.6)	8 (1.9)	
Index offence				
Sexual	96 (8.7)	69 (10.0)	27 (6.5)	4.179 (0.124)
Violent	781 (70.7)	478 (69.6)	303 (72.7)	
Non-violent	227 (20.6)	140 (20.4)	87 (20.9)	
Violence and aggression before the reporting year				
History of harm to others (*n* = 1080)				
No	515 (47.7)	347 (51.6)	168 (41.3)	**10.75 (0.001)**
Yes	565 (52.3)	326 (48.4)	239 (58.7)	
History of harm to objects (*n* = 1080)				
No	743 (68.8)	497 (73.9)	246 (60.4)	**21.23 (< 0.001)**
Yes	337 (31.2)	176 (26.1)	161 (39.6)	
History of harm to self (*n* = 1078)				
No	912 (84.6)	583 (86.6)	329 (81.2)	**5.64 (0.018)**
Yes	166 (15.4)	90 (13.4)	76 (18.8)	
History of verbal aggression (n-1080)				
No	378 (35.0)	265 (39.4)	113 (27.8)	**15.03 (< 0.001)**
Yes	702 (65.0)	408 (60.6)	294 (72.2)	
History of sexual violence (*n* = 1079)				
No	762 (70.6)	492 (73.1)	279 (66.5)	**5.32 (0.021)**
Yes	317 (29.4)	181 (26.9)	136 (33.5)	

** Other diagnoses = substance use disorder (*n* = 6), Personality disorder (*n* = 5), Paraphilia (*n* = 7), anxiety disorder (*n* = 1), traumatic brain injury (*n* = 8)

Figure 1 illustrates the distribution of violent/aggressive incidents alongside polypharmacy. Consistent with the previously mentioned categorical behaviors, individuals experiencing a more significant number of incidents were statistically more likely to be on polypharmacy.

Relationship between recent harm and antipsychotic polypharmacy

In six distinct negative binomial regression models, a significant association between recent aggression/violence and polypharmacy was observed in three instances after adjusting for study covariates: physical harm to objects, self-harm, and verbal aggression (details available in

Table 2 Distribution of polypharmacy across recent violence/aggression incidents

Variable	All participants	Antipsychotic Polypharmacy		χ^2(*p* value)
		No	Yes	
Physical harm to others				
No	944 (85.5)	605 (88.1)	339 (81.3)	**9.59 (0.002)**
Yes	160 (14.5)	82 (11.9)	78 (18.7)	
Physical harm to objects				
No	981 (88.9)	629 (91.6)	352 (84.4)	**13.38 (< 0.001)**
Yes	123 (11.1)	58 (8.4)	65 (15.6)	
Physical harm to self				
No	1063 (96.3)	674 (98.1)	389 (93.3)	**16.88 (< 0.001)**
Yes	41 (3.7)	13 (1.9)	28 (6.7)	
Verbal aggression				
No	811 (73.5)	538 (78.3)	273 (65.5)	**21.96 (< 0.001)**
Yes	293 (26.5)	149 (21.7)	144 (34.5)	
Sexual violence				
No	995 (90.1)	631 (91.8)	364 (87.3)	**6.06 (0.014)**
Yes	109 (9.9)	56 (8.2)	53 (12.7)	

Supplementary Table 3). Patients undergoing polypharmacy were found to have an adjusted incidence rate ratio (IRR) of 1.69 (95% Confidence Interval [CI]: 1.07–2.68; $p = 0.025$) for recent physical harm to objects, indicating they were 1.69 times more likely to exhibit this behavior compared to those not on polypharmacy. Additionally, individuals on polypharmacy had an IRR of 3.30 (95% CI: 1.29–8.44; $p = 0.013$) for self-harming behaviors, suggesting a nearly fourfold increase in likelihood. Furthermore, those on polypharmacy had an IRR of 2.43 (95% CI: 1.35–4.36; $p = 0.003$) for sexually inappropriate behavior, indicating a significantly higher likelihood of exhibiting this behavior. Individuals with polypharmacy were more likely to have an increased likelihood of overall total recent incidents of aggression (IRR = 1.57, 95% CI = 1.10–2.27, $p = 0.014$). See Table 3 for further details.

Discussion

This retrospective study revealed a high prevalence (37.8%) of antipsychotic polypharmacy among forensic psychiatry patients in Ontario, Canada. Polypharmacy was associated with recent incidents of aggression, particularly physical harm to others, self-harm, and sexual violence.

The current study revealed that the prevalence of antipsychotic polypharmacy was 37.8%, which is lower than the 54.9% reported in a retrospective chart review of 142 forensic psychiatry patients from a single hospital in British Columbia, Canada [29]. This discrepancy may stem from the greater diversity of forensic institutions in the current study and the larger and more varied sample size of individuals involved. With multiple institutions involved, prescription practices may differ more than those of a single institution in British Columbia. The sample from Ontario provides a broader patient population with varying levels of severity in their mental illnesses that necessitate antipsychotic polypharmacy use. Additionally, while both are part of the same country, the two forensic systems differ; the one in BC is reportedly more focused on community reintegration and tends to discharge more patients [49]. This may correlate with higher use of antipsychotics in efforts to achieve shorter hospitalization duration stays. In a study of 681 patients from Italian forensic psychiatry, 45.2% were on antipsychotic polypharmacy [30]. This proportion exceeds that found in the current study. The elevated use of polypharmacy could be attributed to the fact that over 35.8% of patients in Residential Mental Health Services (REMS) in Italy experienced aggressive incidents in the month leading up to the study, a rate higher than that in the current research. This suggests a greater reliance on antipsychotic polypharmacy to manage such behaviors [50]. Additionally, medication prescription practices vary widely between countries, with some nations adopting polypharmacy more frequently than others [12]. Moreover, REMS generally operates with less structured oversight than care provided under the ORB, potentially leading to increased polypharmacy usage. Furthermore, patients in the Italian study had a shorter average hospital stay of about 15 months, while the present analysis observed an average of 5 years. This longer duration in the current study may have allowed for more extensive trials with various antipsychotics, resulting in better identification of effective monotherapy options. Finally, the focus of the Italian forensic psychiatric population in REMS on community integration may encourage earlier discharges, which could contribute to an increased use of polypharmacy. However, the prevalence in the current study was slightly lower than 35% among 74 forensic psychiatry patients in Greenland [28]. It is harder to confirm

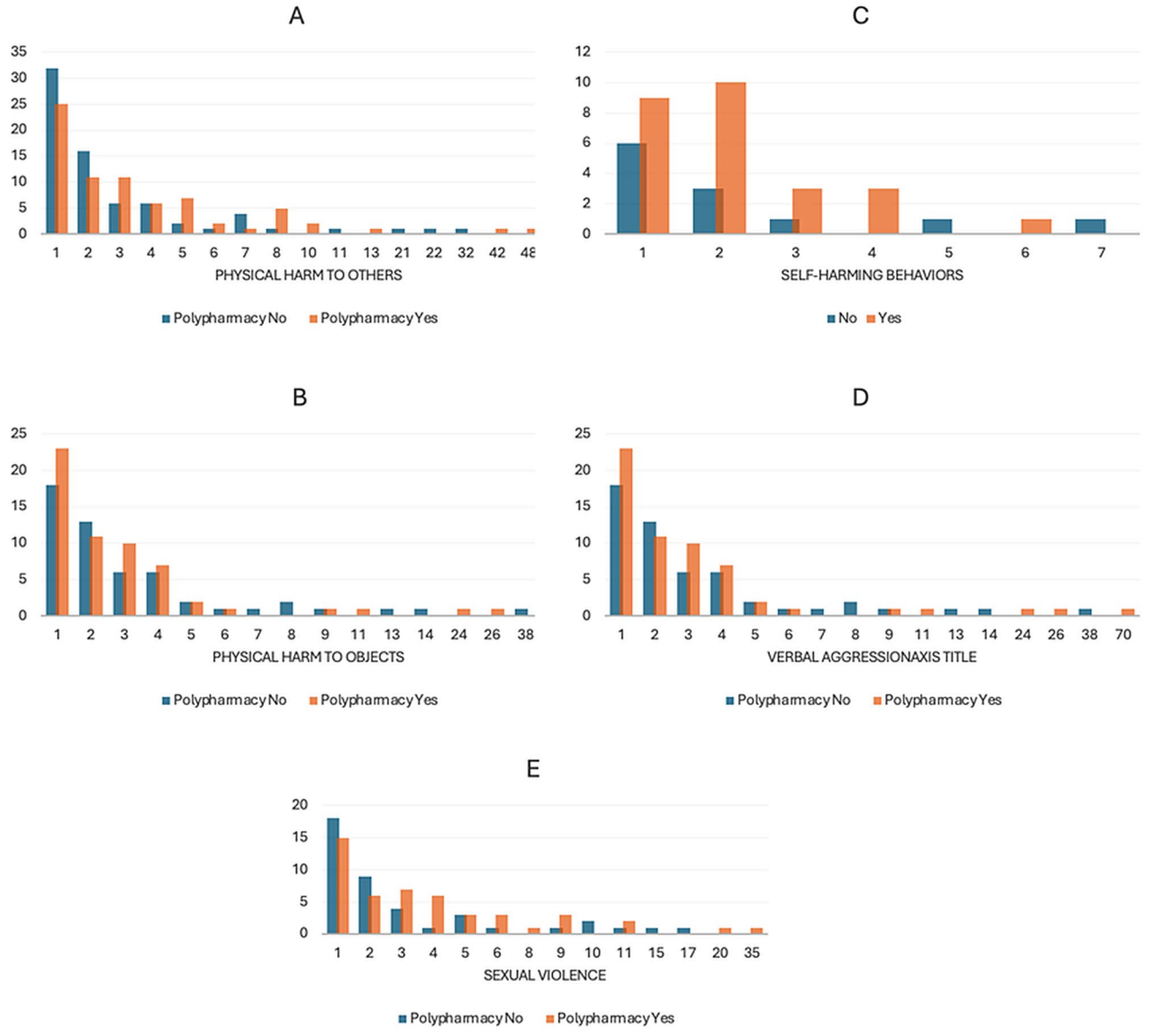

Fig. 1 Distribution of violence/aggressive incidences and polypharmacy

Table 3 Negative binomial regression analysis showing the relationship between recent violence/aggression incidents and antipsychotic polypharmacy

Variable	Bi variable analysis		Multivariable analysis	
	Crude incidence rate ratio (95% confidence interval)	*p*-value	Adjusted incidence rate ratio (95% confidence interval)	*P*-value
Physical harm to others	1.75 (1.05–2.93)	0.010	1.69 (1.07–2.68)	**0.025**
Physical harm to objects	2.15 (1.21–3.86)	0.010	1.69 (0.99–2.90)	0.056
Physical harm to self	1.53 (0.51–4.08)	0.400	3.30 (1.29–8.44)	**0.013**
Verbal aggression	1.45 (0.92–2.26)	0.108	1.25 (0.83–1.88)	0.293
Sexual violence	2.44 (1.28–4.66)	0.518	2.43 (1.35–4.36)	**0.003**
Total recent incidents	1.52 (0.99–2.33)	0.050	1.57 (1.10–2.27)	**0.014**

this similarity since the sample from Greenland was comparatively very small.

This study's finding that individuals on antipsychotic polypharmacy were more likely to exhibit increased overall aggressive incidents, including verbal threats, physical violence, sexual violence, and property damage, aligns with previous research suggesting that polypharmacy is often associated with treatment-resistant patients who present with severe symptoms such as heightened impulsivity and aggression [33, 34]. While polypharmacy is commonly prescribed when monotherapy proves inadequate, the possibility that combined side effects, such as emotional dysregulation, sedation, or akathisia, may contribute to worsening agitation has been raised in earlier studies [51]. However, contrasting evidence suggests that polypharmacy can reduce aggression in specific cases, depending on drug combinations and individual responses [33, 34]. In forensic populations, where patients often have complex mental health conditions, histories of violence, and co-occurring disorders, these findings emphasize the need for tailored treatment plans, close clinical monitoring, and integrated behavioral interventions.

There was a nearly fourfold increase in the likelihood of an increase in physical self-harming incidences among individuals who were on antipsychotic polypharmacy, and this relationship has been observed in forensic and general psychiatry patients [39, 52]. This connection has been previously hypothesized to stem from efforts to control the impulsive symptoms linked to self-harming behaviors [38, 39]. If someone engages in self-harming behaviors, additional antipsychotic medications may typically be prescribed to manage these experiences. However, this aspect could not be assessed in the current analysis because of the cross-sectional nature of the data. Another potential explanation for this relationship is that antipsychotic medications, especially when used in combination, can have significant side effects [37]. These can include increased agitation, akathisia, anxiety, and other mood disturbances through their impact on various neurotransmitters, which might contribute to self-harming behaviors [53, 54]. The interaction between different medications can also exacerbate these side effects, making it more challenging to manage the patient's overall mental health, including self-harming behaviors. Self-harming behaviors are prevalent among individuals diagnosed with borderline personality disorder and related traits [42, 55, 56]. While antipsychotics are sometimes prescribed in clinical practice to manage behavioral dysregulation in this group, there is limited evidence for their efficacy, and clozapine remains the only antipsychotic with stronger evidence in treatment-resistant cases. Consequently, there may be a tendency for healthcare professionals to prescribe more antipsychotic medications as a means of managing these symptoms, often in response to persistent requests from patients, thus this observed relationship between polypharmacy and self-harming behaviors.

Similar to self-harming behaviors, the risk of experiencing sexual violence is reported to be higher in individuals on multiple medications. Studies show that certain antipsychotics, like aripiprazole, may increase the likelihood of hypersexuality, which could result in a greater occurrence of sexual violence when prescribed [57, 58]. However, many antipsychotics also elevate prolactin levels, which are often associated with reduced libido [59–61]. Due to the complex effects of antipsychotics, clinicians may prescribe additional medications to individuals exhibiting violent sexual behavior [62, 63]. This strategy could serve as a form of chemical castration, utilizing the side effects of these drugs to lower libido [63]. In some cases, to effectively manage sexual dysfunction caused by antipsychotics, polypharmacy that includes aripiprazole is suggested, which may contribute to the observed increase in sexual behaviors [64]. It is also important to recognize that sexually violent actions may stem from inadequate control of underlying mental health issues. Therefore, the use of additional antipsychotics might be necessary to manage these behaviors effectively [30, 65]. Given the complexity of these pharmacodynamic effects and the lack of temporal data in this study, we cannot infer causal pathways. More research is needed to clarify these relationships.

Antipsychotics are crucial in managing physical aggression, especially in forensic populations marked by violent behavior and resistant mental health issues. These medications provide sedation, lessen agitation, mitigate psychotic symptoms through dopamine inhibition, and ensure a prolonged calming effect on patients [66]. Such pharmacological interventions are vital for handling acute aggression, particularly when conventional therapeutic approaches fall short [66]. It should be emphasized that atypical antipsychotics are recommended as first-line agents for schizophrenia and related psychotic disorders, not only after conventional antipsychotics fail [67]. Clozapine remains the treatment of choice for treatment-resistant cases [68]. In forensic contexts, patients often exhibit complex behavioral challenges that require comprehensive treatment strategies [69]. It is common for aggressive behaviors to persist even with an adequate dosage of antipsychotic medications prescribed, highlighting the need for polypharmacy. The complexities of primary diagnoses may involve a range of psychiatric disorders, including severe mood dysregulation, paranoia, and comorbid conditions. While polypharmacy is sometimes used in patients with comorbid personality disorder traits, robust evidence for antipsychotics in personality disorders is lacking. Clozapine remains the

only antipsychotic with stronger support in such contexts [70, 71]. Furthermore, polypharmacy may involve clozapine use, notably in cases unresponsive to standard antipsychotic therapies [72]. Clozapine uniquely targets a broader range of symptoms, lowering aggression risks while reducing treatment failure chances, but many individuals end up being on clozapine polypharmacy to manage associated aggressive behaviors [73]. It's important to recognize that aggression in forensic patients is not just a pharmacological issue but is also greatly affected by environmental factors within institutional settings [74, 75]. The dynamics of patient social interactions, provocative behaviors of peers, staff attitudes, and inadequate social support can intensify feelings of frustration and aggression [74, 75]. Thus, aggressive incidents persist to occur despite patients being on polypharmacy. Additionally, differences in metabolism, pharmacodynamic responses, and coexisting conditions like substance abuse can considerably impact antipsychotic effectiveness, leading to treatment-resistant aggression [12, 76].

Limitations

When interpreting the study findings, the following limitations should be considered. Firstly, the study's cross-sectional nature limits our ability to determine causal relationships between antipsychotic polypharmacy and aggressive behaviors; thus, the observed relationships do not necessarily imply direct causation. Furthermore, the reliance on retrospective data raises questions regarding the completeness and accuracy of the records, which could result in distorted findings if essential variables are omitted or inaccurately reported. In addition, the coding of previous violent or aggressive incidents relied on cumulative ORB records, which may vary in detail and accuracy across years. Minor historical events, such as verbal aggression, may have been underreported, inconsistently documented, or subject to reporting bias, which could affect the reliability of these variables. The study also did not consider the dosages of antipsychotic medications, which may greatly impact on the relationship between polypharmacy and aggression, thereby restricting the generalizability of the results. Additionally, focusing solely on Ontario limits the relevance of these findings to other regions, both within Canada and abroad. Also, external factors such as environmental stressors and socio-economic status were not considered, despite their potential independent influence on aggressive behaviors. The timeframe used to evaluate recent aggressive incidents might not reflect the complete range of a patient's behavior, possibly leading to an underestimation of the connection between polypharmacy and aggression. Moreover, using data present in reports can introduce bias since it depends on what message the team wants to communicate, thus eliminating a few vital points. The absence of a control group complicates comparisons between outcomes for those on polypharmacy versus those on monotherapy or no medication. Additionally, the ORB reports did not capture data on adverse effects or treatment-related burden, preventing us from examining whether polypharmacy was associated with increased side effects or poorer tolerability. Lastly, there is no exploration of the long-term effects of polypharmacy on patient outcomes, which leaves a gap in understanding the possible consequences of prolonged antipsychotic use over time. In addition, while the sample size is relatively large, the scope of the available data is limited, capturing only prevalence estimates and associations with aggression without a broader analysis of prescribing patterns or clinical decision-making factors. This restricts the depth of insight that can be drawn and may reduce the standalone contribution of the current findings.

Conclusion

In this study, we observed a significant prevalence of antipsychotic polypharmacy among forensic psychiatry patients, particularly highlighting its association with recent violent and aggressive behaviors. The relationship is heightened in violence to others, themselves, sexual violence, and overall multiple forms of aggression. Although polypharmacy may enhance symptom management for patients exhibiting aggression, it is imperative to consider the potential adverse effects, such as mood disturbances and increased self-aggression. The findings underscore the necessity for clinicians to adopt a cautious approach in prescribing practices, balancing therapeutic benefits against the risks of polypharmacy. Consequently, further research is warranted to explore the nuanced relationship between antipsychotic polypharmacy and aggressive behaviors, ultimately informing evidence-based clinical guidelines that prioritize patient safety and optimal treatment outcomes.

Abbreviations

BC	British Columbia
CI	Confidence Interval
FGA	First-Generation Antipsychotics
HiREB	Hamilton Integrated Research Ethics Board
IRR	Incidence Rate Ratio
NDD	Neurodevelopmental Disorder
NCD	Neurocognitive Disorder
NCR	Not Criminally Responsible due to mental illness
ORB	Ontario Review Board
REMS	Residenze per l'Esecuzione delle Misure di Sicurezza (Italian Residential Mental Health Services)
SD	Standard Deviation
SGA	Second-Generation Antipsychotics
SPSS	Statistical Package for the Social Sciences
UST	Unfit to Stand Trial

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12888-026-07858-9.

Supplementary Material 1

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Author contributions
MMK conceptualizing the research idea. GAC was a vital member of the data collection process. JA and MMK were involved in the data analysis process. MMK drafted the initial manuscript, and GAC, JA, PC, EL, JB, and ATO made substantial intellectual contributions in the subsequent revisions. ATO supervised the various stages involved in writing this current manuscript. ATO and MMK were involved in the visualization of the current manuscript. All authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work.

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Data availability
Due to the sensitivity of the population being explored, the datasets will be made available to appropriate academic parties after approval by GAC.

Declarations

Ethical approval and consent
The Hamilton Integrated Research Ethics Board (HiREB) approved the present study, reference number #15564. The ethics committee/institutional review waived the need for informed consent since the study involved de-identified retrospective data, and individual consent could not practically be obtained. The study was conducted in accordance to the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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