

2022-07-09

Facilitators and barriers to deprescribing antipsychotic medications in critically ill adult patients at transitions of care

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Jaworska, N. (2022). Facilitators and barriers to deprescribing antipsychotic medications in critically ill adult patients at transitions of care (Master's thesis, University of Calgary, Calgary, Canada). Retrieved from <https://prism.ucalgary.ca>.

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Facilitators and barriers to deprescribing antipsychotic medications in critically ill adult
patients at transitions of care

by

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A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES
IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE
DEGREE OF MASTER OF SCIENCE

GRADUATE PROGRAM IN COMMUNITY HEALTH SCIENCES

CALGARY, ALBERTA

JULY, 2022

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ABSTRACT

Antipsychotic medications are prescribed to critically ill adult patients in the intensive care unit (ICU) for clinical indications including delirium, agitation, and sleep disturbances. While there is some evidence for their use in managing agitation, antipsychotic medications have not convincingly shown efficacy for the management of delirium or sleep and are often continued at transitions of care in critically ill patients when they may no longer be necessary or appropriate. The current literature on antipsychotic minimization and deprescribing in critically ill patients is sparse lacking evaluation of underlying facilitators and barriers informing current antipsychotic prescribing practices that may be important in the development of effective minimization and deprescribing strategies. The studies presented in this thesis address knowledge gaps regarding antipsychotic prescribing and deprescribing practices among inpatient healthcare professionals who care for patients with and following critical illness. Based on a qualitative study with semi-structured interviews of 21 healthcare professionals, seven relevant domains from the Theoretical Domains Framework (TDF) contributing to antipsychotic prescribing and deprescribing were identified. A subsequent scoping review of the literature identified differences between healthcare professional perceived and actual prescribing practices, with few in-hospital deprescribing strategies available to guide practice. Thereafter, a nationwide modified Delphi consensus process informed by the qualitative study and scoping review identified consensus statements for antipsychotic minimization activities and antipsychotic deprescribing strategies for patients with and following critical illness. The results of these studies characterize and catalogue relevant priority facilitators and barriers to antipsychotic minimization and deprescribing in critically ill adult patients during their hospitalization to support best clinical prescribing practices.

PREFACE

In this thesis the following three papers have been prepared to be submitted for publication. For each of the included papers, the first author designed and conducted the analyses, interpreted the results, and wrote the manuscript. All three studies were completed with guidance from the senior authors and supervisor. All authors reviewed, critically revised, and contributed intellectually to each of the included papers. The papers are reproduced in their entirety as chapters in this thesis with written permission from all co-authors.

Jaworska N., Krewulak KD., Schlam E., Niven DJ., Ismail Z., Burry LD., Parsons Leigh J., Fiest KM. Facilitators and barriers to deprescribing antipsychotic medications in critically ill adult patients: A qualitative study using the Theoretical Domains Framework. *Prepared for submission.*

Jaworska N., Moss SJ., Krewulak KD., Stelfox Z., Niven DJ., Ismail Z., Burry LD., Fiest KM. A scoping review of perceptions of healthcare professionals on antipsychotic prescribing practices in acute care settings. *Prepared for submission.*

Jaworska N., Makuk K., Krewulak KD., Niven DJ., Ismail Z., Burry LD., Mehta S., Fiest KM. A nationwide modified Delphi consensus process to prioritize experiences and interventions for antipsychotic medication deprescribing among adult patients with and following critical illness. *Prepared for submission.*

ACKNOWLEDGEMENTS

This thesis work could not have been possible without the support of many individuals in the Departments of Community Health Sciences and Critical Care Medicine. I would first like to thank my thesis supervisor, Dr. Kirsten Fiest. Her knowledge, patience, and direction were essential in guiding me to complete this work. I would also like thank my thesis committee members, Dr. Dan Niven and Dr. Zahinoor Ismail. Their insightful comments and lively discussions were influential and crucial to refining this work. Thank you to members of the Fiest team, Dr. Karla Krewulak and Dr. Stephana Moss. Their constant encouragement and invaluable contributions to the completion of this thesis work were vital. Thank you to my colleagues in the Department of Critical Care Medicine who participated in this thesis work and provided the space to complete this work. Lastly, to my friends, family, and husband, thank you for your steadfast support and belief in me. I am deeply grateful for all your encouraging words and conversations.

DEDICATION

This thesis work is dedicated to my husband, Jeffery. Thank you for your unwavering support, encouragement, and pump-up speeches.

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LIST OF SYMBOLS, ABBREVIATIONS, AND NOMENCLATURE

<i>ARDS</i>	Acute Respiratory Distress Syndrome
<i>BMJ</i>	British Medical Journal
<i>COREQ</i>	Consolidated Criteria for Reporting Qualitative Research
<i>CI</i>	Confidence Interval
<i>CINAHL</i>	Cumulative Index to Nursing and Allied Health Literature
<i>COVID-19</i>	Coronavirus Disease 2019
<i>CREDES</i>	Conduction and REporting of DElphi Studies
<i>DSM-5</i>	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
<i>EMBASE</i>	Excerpta Medica dataBASE
<i>ICU</i>	Intensive Care Unit
<i>IQR</i>	Interquartile Range
<i>MEDLINE</i>	Medical Literature Analysis and Retrieval System Online
<i>N</i>	Number
<i>NA</i>	Not Applicable
<i>NREM</i>	Non-Rapid Eye Movement
<i>OR</i>	Odds Ratio
<i>P-value</i>	Probability Value
<i>PICS</i>	Post-Intensive Care Syndrome
<i>PRISMA</i>	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
<i>PRN</i>	Pro Re Nata
<i>PROSPERO</i>	International Prospective Register of Systematic Reviews
<i>PsycINFO</i>	Psychological Information Database
<i>QTc</i>	Corrected QT Interval
<i>SD</i>	Standard Deviation
<i>ScR</i>	Scoping Review
<i>TDF</i>	Theoretical Domains Framework

CHAPTER 1: INTRODUCTION

1.1 Overview of Research Project

This thesis explores the facilitators and barriers to antipsychotic prescribing practices in adult intensive care unit (ICU) patients with and following critical illness using multiple methodologies and data sources to define priority statements related to antipsychotic prescribing minimization and deprescribing activities. This chapter provides background on the topic of antipsychotic medication use in critically ill adult patients and describes current evidence-based best practices for antipsychotic medication prescribing in ICU patients with and following critical illness. This chapter presents current knowledge gaps on antipsychotic medication prescribing in critically ill adult ICU patients and provides justification for the research completed in the subsequent three chapters.

The following three chapters represent: (1) a manuscript prepared for submission for publication; (2) a manuscript prepared for submission for publication; and (3) a manuscript prepared for submission for publication. Each chapter is linked by the theme of the facilitators and barriers to antipsychotic prescribing practices in adult patients with and following critical illness.

A qualitative individual semi-structured interview study was first completed to identify and describe the individual and system factors that influence antipsychotic medication prescribing and deprescribing practices among physicians, nurses, and pharmacists that care for critically ill adult patients during and following critical illness. Subsequently, a scoping review was conducted to characterize antipsychotic medication prescribing practices in acute care settings, to describe perceptions from healthcare professionals on antipsychotic prescribing and deprescribing practices, and to report on antipsychotic deprescribing strategies within acute care settings. The final set of analyses used modified Delphi methodology to synthesize consensus statements on perceptions surrounding antipsychotic prescribing practices, clinical

indications for antipsychotic prescribing, and antipsychotic minimization and deprescribing activities for adult patients with and following critical illness.

This thesis concludes with a discussion of the research findings in the context of current literature, the challenges and limitations of completing this research, clinical and public health implications, directions for future research, and recommendations for the field.

1.2 Aim

The overarching aim of this thesis was to use multiple methodologies to define the factors that contribute to antipsychotic medication prescribing and deprescribing practices in patients with or following critical illness and to synthesize a list of priority items informed by those perceptions and relevant literature to facilitate future in-hospital antipsychotic medication minimization and deprescribing activities.

1.3 Background

1.3.1 Critical Illness

Critical illness encompasses the care of patients that may be facing one of the following life altering or life-threatening circumstances: (1) acute organ dysfunction including those patients that may receive long-term intensive organ support, (2) a major procedure requiring close monitoring to prevent and detect acute organ dysfunction, and (3) a failed trial of intensive care interventions and the delivery of end-of-life care [1]. Critical illness requiring admission to an ICU affects 230,800 Canadian adults per year [2]. Patients who experience critical illness face both short-term and long-term complications due to their acute illness and chronic underlying medical comorbidities [3]. The severity of patient illness, necessary use of sedation,

and additional factors such as immobilization and patient pre-morbid status present a unique set of challenges and risk factors that can impact cognitive and executive functioning of critically ill patients during their hospitalization and in the years following their critical illness [4, 5].

1.3.2 Cognitive Consequences of Critical Illness

ICU-related cognitive impairment affects approximately one third of critically ill adult patients up to 1-year following critical illness with global cognition scores consistent with what would be expected in individuals with mild Alzheimer's disease [6]. This section introduces and explores aspects that influence short-term and long-term cognitive outcomes in ICU survivors and how these complications impact the use of antipsychotic medications, in addition to other sedative medications, in clinical management.

1.3.2.1 Delirium

The *Diagnostic and statistical manual of mental disorders: DSM-5* defines delirium as a disturbance in attention and awareness with additional changes in cognition (e.g., memory deficit, disorientation, poor visuospatial ability) that occurs over a short period of time (i.e., hours to a few days) and represents a change from a patient's baseline functional status with fluctuations during the course of a day [7, 8]. Further, the disturbances are as a direct result of physiological consequences from another medical condition, substance intoxication or withdrawal, or exposure to a toxin [8]. Patients with critical illness are at high risk of developing delirium during their hospital admission [9, 10]. Delirium can manifest with hyperactive symptoms (e.g., agitation, disorientation, aggression), hypoactive symptoms (e.g., sedation, slow motor activity, withdrawal from interactions), or a combination of mixed symptoms [7].

Prior to the implementation of routine monitoring and use of non-pharmacologic strategies for delirium prevention, 60-80% of mechanically ventilated critically ill patients were

reported to experience delirium during their ICU admission [2, 7, 11]. With current strategies commonly adopted in many ICUs globally that promote the use of validated diagnostic tools for the recognition of delirium and implement protocols to reduce oversedation and immobility, the prevalence of delirium among critically ill patients is now reported to be approximately 30% [10, 12]. Developing delirium in the ICU carries significant risks for negative patient outcomes. Delirium has been consistently shown to independently increase the risk of mortality, increase duration of mechanical ventilation, and increase the time spent in ICU and hospital [10, 11, 13]. Several environmental and iatrogenic risk factors including the use of benzodiazepines and opioid medications, sleep disturbances due to excessive light and noise at night, and sedative-associated coma have been identified as potentially modifiable factors for reducing the incidence of delirium [5, 14, 15].

The underlying pathophysiology of delirium is not well understood with several hypotheses proposed describing alteration in neurotransmitter pathways thought to be responsible for delirium [16]. Current hypotheses propose multifactorial pathophysiological mechanisms including neuronal oxidative stress and reduced cerebral oxidative metabolism, direct neurotoxic effects of inflammatory cytokines, and changes in neurotransmitters that regulate behaviour, mood, and cognition (e.g., dopaminergic, serotonergic, and gamma-aminobutyric acid pathways, alpha-2 pathways) [17, 18]. Pharmacologic interventions for delirium have understandably targeted these neurotransmitters attempting to modulate the cognitive symptoms of delirium and/or behavioural symptoms such as agitation. It is important to note that current evidence identifies non-pharmacologic strategies (i.e., ABCDEF bundle) as best clinical practice for the prevention and reduction of the duration of delirium when comprehensively implemented [19, 20]. Despite the evidence for non-pharmacologic interventions for delirium prevention and management, pharmacologic strategies – largely focused on antipsychotic medications – remain common management interventions for symptoms related to delirium and/or agitation. Antipsychotics tend to be still widely prescribed

for delirium particularly when associated with symptoms of agitation with limited evidence for efficacy and certain risk for excessive sedation and other adverse events (e.g., QTc prolongation, falls) [21, 22]. Implementation of evidence-based non-pharmacologic strategies (i.e., ABCEDF bundle) has been encouraging, however challenges with antipsychotic prescribing remain due to the high resource requirements needed to administer all recommended aspects of non-pharmacologic strategies (e.g., physiotherapy, additional nursing presence) [19, 23].

1.3.2.2 Sleep Disturbances

Sleep disturbances and poor sleep frequently occur in the ICU [24]. Sleep disturbances are defined broadly as any changes from normal sleep quality (e.g., architecture, fragmentation), quantity (e.g., latency, duration), or circadian rhythm [24]. These disturbances during critical illness have been associated with cognitive impairment and psychologic distress [25]. Patient-reported precipitating physiologic factors for sleep deprivation include pain and discomfort among the most common contributors to poor sleep quality [24]. Patients additionally experience psychological distress in the form of worry, anxiety, and fear that impacts their sleep quality while admitted to the ICU [24]. Specific ICU environment and pharmacologic factors impact sleep disruption. Ambient noise in the ICU from staff conversations and alarms and exposure to mechanical ventilation are commonly reported by patients to subjectively disrupt sleep [25, 26]. Exposure to ICU-specific medications such as benzodiazepines and propofol may also have negative impacts on sleep quality and architecture increasing total sleep time but resulting in abnormal sleep architecture [26, 27].

The relationship between sleep disturbances and delirium is likely bidirectional with sleep deprivation contributing to delirium and delirium occurrence potentiating sleep disturbance [25]. The interplay between sleep, delirium, and sedative use in the ICU remains unclear and under investigated [27]. However, sleep fragmentation likely worsens at least short-term

cognitive impairment as recently identified by Wilcox and colleagues [28]. Interest in the contribution of sleep disturbance to the incidence of delirium has been increasing but evaluation of potential pharmacologic interventions for sleep disturbances continues to lag.

Antipsychotic medications are still commonly used in the ICU and their use in pharmacologic sleep management is sparsely documented within the literature. Mechanistic understanding of antipsychotic pharmacologic properties has likely been extrapolated for use in sleep management, however limited data are currently available to advocate for the routine use of antipsychotic medications for the promotion of sleep quality and quantity. Typical antipsychotics such as haloperidol antagonize dopamine receptors and increase stage 3 nonrapid eye movement (NREM) sleep, important for deep regenerative sleep [25, 29]. Atypical antipsychotics such as quetiapine, risperidone, and olanzapine have additional affinity for serotonergic, muscarinic, and histaminergic receptors with varying binding profiles [30]. Their histaminergic binding properties are likely responsible for the increase in total sleep time, sleep efficiency, and stage 2 NREM sleep responsible for the transition to deep sleep (i.e., Stage 3 NREM) [25, 29, 30]. Multicomponent intervention protocols focused on non-pharmacologic sleep promotion and reduced reliance on pharmacologic sleep aids have been promising in improving sleep quality and reducing the incidence of delirium [31, 32]. However, widespread implementation remains challenging due to the required cultural and behavioural shifts coupled with challenging clinical circumstances (e.g., nocturnal agitation and/or aggression) that reduce broad adherence [25].

1.3.2.3 Long-term Cognitive Impairment

Long-term cognitive impairment in critically ill patients, which encompasses memory impairment, inattention, and reduced executive functioning, is exceedingly common [4, 9]. Critically ill patients face a high risk of long-term cognitive impairment following their critical illness, with worse global cognition and executive functioning following hospital discharge [6].

This cognitive impairment appears to improve over time, but for a subset of patients these symptoms may persist without improvement. For example, acute respiratory distress syndrome (ARDS) survivors are at particular risk of cognitive impairment with 70-100% of patients having persistent cognitive impairment symptoms at hospital discharge [33, 34]. Twenty percent of these patients show ongoing symptoms of cognitive impairment up to five years later [3].

Several modifiable risk factors have been identified that increase the risk of critically ill patients developing long-term cognitive impairment. These risk factors include ICU delirium and its duration, hypoglycemia, and sedation [4, 35]. Delirium phenotypes, specifically sedative-associated, hypoxic, and septic delirium, have been associated with worse long-term cognitive impairment up to one year following hospital discharge [35]. Among delirium phenotypes, sedative-associated delirium is the most common with 64% of critically ill delirious patients in one prospective cohort study experiencing sedative-associated delirium [36]. When present with prolonged duration sedative-associated delirium has been associated with the greatest negative change in global cognition scores at both three months and 12 months among all delirium phenotypes [36].

Little is known about how antipsychotic medications, which have significant sedating side effects, contribute to sedative-associated delirium and in turn long-term cognitive impairment. Antipsychotic medication continuation following hospitalization for critical illness is common, and in non-critically ill older patients it is associated with greater cognitive impairment and somnolence [37, 38]. To date, evaluation of specific sedative medications in the association of sedative-associated delirium and long-term cognitive impairment have failed to account for the exposure of antipsychotics during ICU admission as well as continuation of antipsychotics following hospitalization [36].

1.3.3 Current Evidence for Antipsychotic Medication Use for Delirium and Agitation in the ICU

Over the past several decades, pharmacologic agents – particularly antipsychotic medications – have gained acceptance and are now commonly used in the management of the anxiety-provoking symptoms of delirium and/or agitation [20]. The evidence to support this clinical practice has evolved over time with an increasing collection of interventional studies calling into question the clinical efficacy of a number of these medications [17]. This section introduces and reviews some aspects of the current evidence on several pharmacologic agents commonly used for the management of the symptoms of delirium and/or agitation in the ICU.

1.3.3.1 Haloperidol

Haloperidol, a dopamine antagonist typical antipsychotic, has been readily available for clinical use since 1967 [39, 40]. The administration of haloperidol for the prevention and/or management of the symptoms of delirium related to critical illness has been extensively investigated with multiple randomized control trials in various critically ill patient populations [21, 41-43]. Page and colleagues evaluated the efficacy of scheduled haloperidol compared to placebo in the prevention of delirium in 142 critically ill patients either at risk of developing delirium or already displaying symptoms of delirium in a randomized double-blind control trial study design [21]. The researchers found no significant difference between groups with respect to days with delirium or confusion; however, significant adverse effects were reported in the group receiving haloperidol, including QTc prolongation and over sedation [21]. Van den Boogaard and colleagues further evaluated the impact of scheduled prophylactic haloperidol at 1mg and 2mg doses every 8-hours compared to placebo on 28-day survival in critically ill patients at high risk of developing delirium [42]. The trial was stopped prematurely after randomizing 1789 patients after meeting their threshold for futility for the primary outcome of 28-day survival. Expectedly, there was no difference in the incidence of delirium between those receiving any haloperidol dose and placebo [42]. Finally, Girard and colleagues evaluated the

effect of haloperidol on delirium duration in a 1183 patient three-arm double-blind placebo control trial – ziprasidone versus haloperidol versus placebo [41]. The median number of days alive without delirium or coma did not differ between haloperidol and the placebo groups [41]. To date, no interventional studies have consistently shown that haloperidol impacts the incidence or duration of delirium [17].

1.3.3.2 Quetiapine

Evaluation of the efficacy and safety of quetiapine for critical illness related delirium was first explored by Devlin and colleagues with a small double-blind multicenter pilot randomized control trial of 36 patients randomly allocated to receive quetiapine or placebo [44]. Although the duration of delirium was found to be shorter, with less agitation among the patient group who received quetiapine, there are limitations to this study beyond its small sample size worth noting [44]. Multiple statistical tests increased the risk that the study results were a type I error. Additionally, only 14% of patients that were screened for inclusion were ultimately enrolled in the study due to meeting exclusion criteria (i.e., prior antipsychotic use within 30 days, not receiving enteral nutrition, primary neurological condition) suggesting limited generalizability in the study outcomes for patients with new onset delirium and/or agitation. As one of the first studies of atypical antipsychotic use for delirium in critically ill patients that suggested clinical efficacy in reducing delirium duration, quetiapine use for delirium has become commonplace.

The frequent use of quetiapine has spurred investigation into the quetiapine parenteral equivalent drug, ziprasidone [41]. As previously described, Girard and colleagues evaluated the efficacy of ziprasidone (and haloperidol in a separate study arm) on delirium duration in a large randomized double-blind control trial. As the first parenteral atypical antipsychotic approved in the United States, ziprasidone has several similarities to quetiapine, its oral medication alternative. Ziprasidone has a high affinity binding for the serotonergic receptors, modest reuptake inhibition of norepinephrine, and a low incidence of extrapyramidal symptoms [45].

Like the results found in the haloperidol study arm, no difference in delirium duration was identified with the administration of ziprasidone compared to placebo [41]. This large-scale study has provided the most reliable evidence to date showing the lack of clinical benefit of this atypical antipsychotic group on delirium duration and raises the question of atypical antipsychotic use in this patient population.

1.3.3.3 Risperidone

Sparse data exists surrounding the use of risperidone in critically ill patients with delirium. The administration of risperidone in non-critically ill patients with delirium has been more extensively studied. Several small randomized control trials with hospitalized adult patients have evaluated the efficacy of risperidone on delirium duration and incidence [46]. A recent systematic review and network meta-analysis of pharmacologic interventions for delirium – including both critically ill and hospitalized patients – suggested that risperidone was not associated with a delirium treatment response (odds ratio (OR) 1.57 (95% confidence interval (CI) 0.56 – 4.38)) but was associated with reduced odds of delirium incidence (OR 0.27 (95%CI 0.07 – 0.99) [46]. However, the precision of this effect estimate may be poor due to the small sample sizes across included studies. Although only scarce evidence continues to exist to support the use of risperidone among critically ill patients with delirium, up to 5% of critically ill patients in at least one observational study received risperidone as a pharmacologic treatment for delirium [38]. Healthcare professionals may be extrapolating the clinical efficacy and safety outcomes of other antipsychotics to justify the utilization of risperidone among critically ill patients with delirium.

1.3.3.4 Olanzapine

One small study exploring the administration of olanzapine for the management of the symptoms of delirium in critically ill adults remains the only interventional study aimed at understanding the efficacy of olanzapine on delirium duration [47]. Skrobik and colleagues compared the safety and estimated clinical response of olanzapine or haloperidol (placebo group) in critically ill adults with delirium in an unblinded randomized trial. In the study, 103 critically ill patients with delirium were randomized to receive doses of haloperidol or olanzapine within two hours of the diagnosis of delirium being made [47]. Although the results suggest that olanzapine is at least as effective at managing the symptoms of delirium as haloperidol, there are several limitations to this study and risks of bias. Not only was the study sample size small, but there was also uneven distribution of patients between the two treatment groups, and a lack of blinding of nurses and physicians diagnosing delirium and administering medications. Finally, the definition of delirium presence was not standardized due to historic definitions of delirium. Despite this study which is now nearly two decades old, there have not been any larger studies of olanzapine use in the critical care environment to inform current antipsychotic clinical practices.

1.3.4 Antipsychotic Medication Prescribing Practices in the ICU

Antipsychotic medications remain by far the most prescribed agents for delirium, with up to 42% of patients receiving an antipsychotic medication while in the ICU [38]. However, the lack of clinical efficacy of antipsychotics in the management of delirium has led to questioning of this common clinical practice [17, 41, 42, 47-49]. Several retrospective cohort studies have reported on the prevalence of antipsychotic medication prescribing in critically ill patients for delirium management. These studies have shown that between 23% and 45.6% of critically ill patients are newly prescribed an antipsychotic medication during their ICU admission [38, 50, 51]. Within the Canadian context, antipsychotic medication use in critically ill patients is reported

to be 16.2% in one prospective cohort study [52]. This may be an underestimate of the true prevalence of antipsychotic medication use due to inconsistent reporting of delirium and prescribing records.

The Society of Critical Care Medicine, the largest international medical organization representing the practice of critical care medicine, has outlined guidelines surrounding the use of antipsychotic medications for patients experiencing agitation and delirium [20, 53]. Current guideline recommendations advocate against the routine use of antipsychotic medications for the prevention or treatment of delirium [20]. The use of antipsychotic medications is increasingly recognized to not improve important patient-centered outcomes; their use does not lower the incidence of delirium, nor does it shorten the duration of delirium [21, 41-43]. Further, antipsychotic use does not shorten duration of mechanical ventilation, ICU length of stay, or lower mortality [20]. However, clinical circumstances do occur where short-term antipsychotic use may be necessary in the critically ill delirious patient because of severe agitation from anxiety or hallucinations that places them at risk of harm to themselves or others [20]. This may be an important and underrecognized factor contributing to why current clinical practice guidelines on antipsychotic medication prescribing for delirium and/or agitation may not be readily followed or implemented.

Up to 30% of patients prescribed an antipsychotic medication in the ICU will subsequently be discharged from hospital with an ongoing prescription without a clinical indication for ongoing use [38, 54]. Risk factors for discharge on a new antipsychotic medication following admission to the ICU include increased severity of illness, exposure to benzodiazepine drugs, and quetiapine exposure which is a commonly prescribed oral antipsychotic [38, 51, 55]. Long-term antipsychotic medication use is associated with increased risk of sudden cardiac death, falls, and worsening cognitive impairment [6, 35]. Restrictive prescribing guidelines (i.e., authorization requirements for prescribing, specialized prescribers) of antipsychotics are unlikely to be effective or safe approaches to curb utilization of these medications due to clinical

necessity and limited alternative agents [56]. Collaborative multidisciplinary efforts to modify antipsychotic prescribing practices are needed to promote rational deprescribing of these medications during the hospitalization of this patient population. Understanding prescribing practices and promoting deprescribing of antipsychotic medications prior to hospital discharge is important to avoid adverse events and improve quality of life [35].

1.3.5 Deprescribing Practices in the ICU

Deprescribing is “the process of withdrawal of an inappropriate medication, supervised by a healthcare professional with the goal of managing polypharmacy and improving outcomes” and currently remains an uncommon practice in the ICU environment [57]. Evidence on facilitators and barriers to deprescribing antipsychotic medications has focused predominantly on the primary care environment [58]. Two recent studies have evaluated antipsychotic deprescribing interventions in the ICU. A pre-post quality improvement initiative of 358 critically ill patients receiving antipsychotic medications evaluating the efficacy of a pharmacy-initiated electronic handoff tool did not find a statistically significant reduction in antipsychotic medication prescribing at time of ICU transfer [59]. In their intervention, an ICU clinical pharmacist generated an electronic handoff that would flag the antipsychotic for daily follow-up and made recommendations for deprescribing in the ICU and on the ward if necessary. Poor compliance and a lack of rationale for use of their tool among participants likely contributed to the negative study outcome [59]. In the second intervention study, the authors performed a pre-post retrospective study of 140 critically ill patients evaluating an antipsychotic discontinuation bundle within the ICU [60]. The antipsychotic discontinuation bundle included a multidisciplinary bimonthly education program and a discontinuation algorithm outlining thresholds for safe dose down titration and discontinuation. A significant reduction in the proportion of patients that continued on an antipsychotic medication upon ward transfer was found. Although an encouraging study supporting feasibility, the complexity of their deprescribing algorithm, small

sample size, and retrospective design calls for further studies driven to identify simpler, targeted interventions with prospective study designs to address deprescribing antipsychotics among patients with and following critical illness.

1.4 Knowledge Gap and Significance

The field of critical care medicine has made incredible progress over the last two decades in the understanding of delirium and agitation and the role of antipsychotics in the management of delirium and agitation. It has become clear that antipsychotics do not improve patient-centered outcomes [20]. Little remains known as to the impact of antipsychotic medications for the management of sleep disturbances in critically ill patients. A disconnect remains between the catalogue of high-quality literature produced on the clinical efficacy of antipsychotic medications in adult patients with critical illness and current clinical practices within the ICU environment. The important factors informing why healthcare professionals continue to prescribe and utilize antipsychotics despite strong evidence on patient-centered outcomes has remained unclear in the literature. Previous studies on understanding the facilitators and barriers to the adoption of high value practices and de-adoption of low-value clinical interventions in the ICU have identified a lack of knowledge, ICU culture, absence of clinical guidelines, and provider behaviour as contributors to prescribing practices [61]. Knowledge deficiency may only be a minor contributor to antipsychotic prescribing practices as structure, process, and outcome factors are more commonly reported as relevant factors in the adoption and de-adoption of practices in the ICU environment [61]. Structure, process, and outcome factors that influence healthcare professional medication prescribing and deprescribing behaviours remain largely uninvestigated, limiting the opportunity to identify interventions to accelerate antipsychotic minimization and deprescribing practices. The current literature on antipsychotic minimization and deprescribing is sparse and lacks methodological rigor in the

evaluation of the underlying facilitators and barriers to antipsychotic deprescribing that are important to developing effective minimization and deprescribing strategies. Bringing together perspectives from multidisciplinary stakeholders, mapped to the current available literature, is necessary to advance the foundational knowledge needed to develop, implement, and evaluate future pragmatic interventions aimed at enhancing patient safety and decreasing adverse drug events related to antipsychotic overprescribing. The studies presented in this thesis address these knowledge gaps.

1.5 Objectives

1.5.1 Objective 1

Describe relevant factors that influence antipsychotic prescribing and deprescribing practices among physicians, nurses, and pharmacists that care for critically ill adults during and following critical illness.

1.5.2 Objective 2

Map the literature on antipsychotic medication prescribing and deprescribing practices in acute care, describe healthcare professional perceptions on antipsychotic prescribing and deprescribing practices, and report on antipsychotic deprescribing strategies within acute care.

1.5.3 Objective 3

Synthesize a list of priority statements on antipsychotic minimization strategies and antipsychotic deprescribing activities for adult patients with and following critical illness.

The above objectives were achieved by completing three studies. For objective 1, a qualitative study with individual semi-structured interviews of physicians, nurses, and pharmacists that care for adult patients with or following critical illness was conducted and is reported in Chapter 2. Chapter 3 addresses objective 2 and describes the results of a scoping review by reporting on antipsychotic prescribing practices in acute care settings including both prescribing and deprescribing and the perceptions of healthcare professionals on their antipsychotic prescribing practices. Finally, Chapter 4 addresses objective 3 presenting the results of a nationwide modified Delphi consensus process engaging healthcare professionals in their perceptions on antipsychotic prescribing and deprescribing in adult patients with and following critical illness to develop a list of priority statements aimed at identifying potential strategies for antipsychotic minimization and deprescribing.

1.6 Thesis Outline

This thesis discusses facilitators and barriers to antipsychotic minimization and deprescribing strategies in adult patients with and following critical illness. In the current Chapter, Section 1.1 reviews the overall aim of this thesis. Section 1.3 gives background information for this thesis; explicitly Section 1.3.1 describes the cognitive consequences of critical illness, Section 1.3.2 reviews current evidence for antipsychotic medication use for delirium and agitation in the ICU, Section 1.3.3 explores antipsychotic medication prescribing practices in the ICU, and Section 1.3.4 discusses deprescribing practices in the ICU. Section 1.4 presents the knowledge gaps and significance of this thesis work, followed by Section 1.5 addressing thesis objectives and the current section which provides a broad thesis outline.

Chapter 2, 3, and 4 each present a scholarly journal article prepared for submission for publication. These papers represent the main body of the thesis and include: (1) a qualitative study describing relevant factors that influence antipsychotic prescribing and deprescribing

practices among physicians, nurses, and pharmacists that care for critically ill adults during and following critical illness; (2) a scoping review characterizing antipsychotic medication prescribing and deprescribing practices, healthcare professional perceptions on antipsychotic prescribing and deprescribing practices, and antipsychotic deprescribing strategies within acute care; and (3) a nationwide Delphi consensus process that provides a list of priority statements on antipsychotic minimization strategies and antipsychotic deprescribing activities for adult patients with and following critical illness.

Chapter 5 presents a discussion of the relationship between the factors influencing antipsychotic prescribing practices and the broader implications on the care of critically ill patients with delirium and/or agitation. Section 5.1 summarizes the main findings of each paper followed by Section 5.2 which places the study findings in the context of existing literature. Section 5.3 describes challenges and limitations in studying antipsychotic prescribing practices in critically ill patients. Section 5.4 presents clinical public health implications of this thesis work, and Section 5.5 delves into directions for future research. Section 6.6 explores recommendations for the field of critical care medicine in relation to this thesis work followed by Section 6.7 which concludes this thesis.

**CHAPTER 2: FACILITATORS AND BARRIERS TO DEPRESCRIBING
ANTIPSYCHOTIC MEDICATIONS IN CRITICALLY ILL ADULT PATIENTS: A
QUALITATIVE STUDY USING THE THEORETICAL DOMAINS FRAMEWORK**

Jaworska N., Krewulak KD., Schlam E., Niven DJ., Ismail Z., Burry LD., Parsons Leigh J., Fiest KM. Facilitators and barriers to deprescribing antipsychotic medications in critically ill adult patients: A qualitative study using the Theoretical Domains Framework. *Prepared for submission.*

2.1 Abstract

Background: Antipsychotic medications do not alter the incidence or duration of delirium, but these medications are frequently prescribed and continued at transitions of care in critically ill patients when they may no longer be necessary or appropriate. The purpose of this study was to identify and describe relevant domains and constructs that influence antipsychotic medication prescribing and deprescribing practices among physicians, nurses, and pharmacists that care for critically ill adult patients during and following critical illness.

Methods: We conducted semi-structured interviews with critical care and ward healthcare professionals including physicians, nurses, and pharmacists to understand antipsychotic prescribing and deprescribing practices for critically ill adult patients during and following critical illness. We used deductive thematic analysis using the Theoretical Domains Framework (TDF) to identify and describe constructs within relevant domains.

Results: Twenty-one interviews were conducted with 11 physicians, five nurses, and five pharmacists. Seven TDF domains were identified as relevant from the analysis:

Social/professional role & identity; Beliefs about capabilities; Reinforcement; Motivations & goals; Memory, attention & decision processes; Environmental context & resources; and Beliefs about consequences. Participants report antipsychotic prescribing for multiple indications beyond delirium and agitation including patient and staff safety, sleep management, and environmental factors such as staff availability and workload. Participants identified potential antipsychotic deprescribing strategies to reduce ongoing antipsychotic medication prescriptions for critically ill patients including direct communication tools between prescribers at transitions of care.

Conclusions: Critical care and ward healthcare professionals report several factors influencing established antipsychotic medication prescribing practices that aim to maintain patient and staff

safety in order to facilitate providing care to patients with delirium and agitation limiting adherence to current guideline recommendations.

2.2 Introduction

Delirium is a common complication of critical illness among adult patients for which antipsychotic medications are frequently prescribed to reduce agitation symptoms [1-4]. However, large randomized controlled trials have shown that antipsychotic medications do not alter the incidence or duration of delirium among most critically ill patients [5-9]. In 2018 the Society of Critical Care Medicine updated their Clinical Practice Guidelines on the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption recommending against the routine use of antipsychotic medications for delirium [10]. Adoption of this recommendation remains challenging due to the clinical burden of delirium and agitation, lack of effective alternative pharmacologic interventions to manage agitation symptoms, and lack of clear, delirium-domain targeted approaches for pharmacologic interventions [6, 11, 12]. Patients prescribed antipsychotic medications in the ICU are often discharged from hospital with an ongoing antipsychotic prescription that may no longer be necessary [13-16]. Utilizing a systematic approach to understand behavioural and socioenvironmental factors influencing antipsychotic prescribing practices may enhance interventions to more effectively and sustainably ensure antipsychotic medications are not unnecessarily continued at hospital discharge.

We utilized the TDF, a 14-domain behaviour change framework, to understand individual- and hospital-level factors that influence antipsychotic prescribing practices among healthcare professionals involved in the prescribing and deprescribing of antipsychotic medications in critically ill adults [17, 18]. The objectives of this study were to: (1) identify relevant domains that influence antipsychotic prescribing practices among physicians, nurses,

and pharmacists that care for critically ill adults during and following critical illness; (2) describe constructs within relevant domains related to antipsychotic prescribing practices; and (3) catalogue potential deprescribing strategies identified by participants for future in-hospital deprescribing initiatives.

2.3 Methods

2.3.1 Study Design

This qualitative study is reported according to the Consolidated Criteria for Reporting Qualitative Research checklist (**Table 2.1**) [19]. Interviews were conducted between July 6 and October 29, 2021. The study was approved by the University of Calgary Conjoint Health Research Ethics Board (REB21-0963).

2.3.2 Participant Selection

Participants were eligible if they were Alberta physicians, nurses, or pharmacists who spoke English, had a clinical appointment within the hospital environment within the last five years, and provided care to critically ill adult patients (i.e., ICU) or patients following critical illness (i.e., on the hospital ward). Participants were recruited using convenience and snowball sampling with eligible participants recruited through social media posts and email invitations. All participants provided informed consent prior to participation.

2.3.3 Data Collection

Interview guides were developed by the research team and informed by previous interview guides using the TDF within critical care [20]. (**Appendix 2.1 – 2.3**) Interview guides were piloted with an ICU physician, ICU nurse, and ICU pharmacist prior to their administration. Participants were emailed objectives of the study and a consent form detailing the interview

process. One researcher (NJ) trained in qualitative methods conducted all interviews individually with participants over Zoom (Zoom Video Communications, Inc., San Jose, United States). The researcher conducting interviews (NJ) is a critical care physician who had a previous relationship with eight physicians, one nurse, and four pharmacists through clinical work. Interviewer bias was addressed by re-iterating a non-judgemental, confidential environment prior to interview initiation and avoidance of leading questions [21]. The professional relationship of the interviewer provided a collegial and empathizing environment for participants given a commonality of understanding of clinical circumstances and challenges. Interviews ranged from 30 to 60 minutes. Interviews were audio-recorded for subsequent verbatim transcription. Field notes were made during and after the interview and were revisited between interviews. To ensure credibility, participants were emailed a summary of their interview responses for review, comments, and corrections to ensure their perspectives were accurately interpreted. Nine participants responded with confirmation of accuracy and one participant sent corrections.

2.3.4 Data Analysis

Verified and de-identified transcripts and interview summary comments were imported into Nvivo12 (QSR International, Melbourne, Australia) for data analysis. Three female researchers (NJ, KDK, ES) trained in deductive qualitative analysis using the TDF framework completed all data analysis. Three researchers (NJ, KDK, ES) analyzed data using deductive thematic analysis informed by the TDF, following the outlined multi-step approach: 1) read text transcripts line-by-line to identify responses and develop a codebook to categorize responses into TDF domains (**Table 2.2**); 2) develop beliefs from identified responses within their assigned domains. A belief was defined as a collection of responses comprising a similar theme that focused on the problem of ongoing antipsychotic medication prescribing and/or addressed an influence on the target behaviour of antipsychotic deprescribing [20]; 3) analyze the beliefs from the domains to identify discrete constructs from the TDF within each domain; and 4) select

relevant theoretical domains from the TDF based on their frequency within transcripts, presence of conflicting beliefs, and presence of strong beliefs that could impact behaviours [17, 18, 20, 22]. Each transcript was coded independently and in duplicate. To address rigor, the researchers utilized cross-examination by having the same transcript reviewed by researchers from different disciplines and backgrounds (e.g., clinicians, researchers). Dependability and confirmability were addressed by maintaining an audit trail and through iterative coding meetings during each data analysis step to clarify coding differences when establishing identified domains. During analysis, the researchers provided reflective commentary to challenge possible conclusions and minimize the risk of bias. Data analysis and data collection occurred in parallel to understand and apply derived codes and constructs to transcripts as new information was garnered. Saturation was achieved across all domains for each healthcare professional role following 21 interviews when all themes were identified in all healthcare professional role interviews and no new beliefs were identified.

2.4 Results

We completed 21 interviews with 11 physicians, five nurses, and five pharmacists. Thirteen (62%) participants worked primarily in the ICU and 8 (38%) participants worked primarily on hospital wards. Participants were recruited from six medical centres with 20 (95%) working in an academic environment. Participant characteristics can be found in **Table 2.3**. Four participants were recruited via social media (i.e., Twitter) and 12 from the researchers' personal contacts. Five participants were recruited through snowball sampling from participants forwarding study information to their networks.

2.4.1 Domains Relevant to Antipsychotic Prescribing Practices

Seven of 14 theoretical domains (n=7/14; 50%) and related constructs were relevant to antipsychotic prescribing practices for healthcare professionals (**Figure 2.1**). **Table 2.4** provides a detailed collection of all relevant and non-relevant domains, constructs, and identified beliefs from participants.

Exemplar quotations for all domains and constructs enumerated below are available in **Table 2.5**.

2.4.1.1 Social/Professional Role & Identity

The researchers identified three constructs in the domain *Social/professional role & identity*: professional identity/boundaries/role, professional confidence, and group identity. Healthcare professionals shared their commitment to attempting non-pharmacologic interventions prior to utilizing antipsychotic medications, however there were differing views regarding utilization of antipsychotic medications when non-pharmacologic management was perceived to be ineffective. In these circumstances, most nurses saw their role as patient advocate (**Q1**). Pharmacists and physicians more commonly referred to their professional confidence surrounding antipsychotic medication prescription monitoring and safe prescribing practices. One ward physician commented, “we really only prescribe the medications with very specific disclaimers if we are going to use low-dose PRN [*pro re nata*] antipsychotics, and usually we prescribe them kind of with a disclaimer which says something like, “This is only to be used for significant agitation or aggression which is putting the individual patient or others at risk of harm.”” All healthcare professionals perceived that antipsychotic prescribing was aligned with their centre’s accepted prescribing practices but highlighted the existence of interdepartmental and individual prescribing differences.

2.4.1.2 Beliefs About Capabilities

The researchers identified five constructs in the domain *Beliefs about capabilities*: beliefs, perceived competence, perceived behavioural control, professional confidence, and empowerment. Some healthcare professionals representing all roles reported holding beliefs around the usefulness of antipsychotics and being the preferred medication due to safer sedation effects. In contrast, some healthcare professionals described their belief of the inefficacy of antipsychotics with one ward nurse commenting on their use for agitation, “I’m not convinced that antipsychotics really help with that in all instances.” Healthcare professionals described perceived behavioural control as variable adherence with known literature on antipsychotic prescribing and efficacy. One ICU pharmacist stated, “we’re all aware of some of the conflicting data out there, but I don’t know that they’re [*physicians*] specifically following guidelines every time that they’re prescribing the antipsychotics.” Additionally, healthcare professionals perceived they were participating in antipsychotic deprescribing practices at transitions of care with ward healthcare professionals speaking more directly to their commitment to deprescribing practices than ICU healthcare professionals (**Q2**). ICU physicians felt professional confidence in their individual antipsychotic prescribing practices and drug administration competency. In contrast, ward physicians described professional confidence in their role of managing deprescribing of antipsychotic medications following patient transfers from the ICU to the ward. ICU nurses but not ward nurses described empowerment in requesting antipsychotic medications as a pharmacologic intervention, particularly during night shifts (**Q3**).

2.4.1.3 Reinforcement

The researchers identified three constructs in the domain *Reinforcement*: incentives, reinforcement, and consequents. The most reported incentives related to antipsychotics prescribing were patient and staff safety (**Q4**). This practice was discussed more frequently in

the ICU than the hospital ward. As one physician reported, “in the ICU, unless the patient is exhibiting significant agitation that it’s becoming a safety issue, it’s important for me to try and not prescribe an antipsychotic, and especially once a patient’s out of the ICU, my threshold becomes even higher to prescribe an antipsychotic.” Antipsychotic prescribing practices were further reinforced by patient volume and workload (Q5) and the perceived variable efficacy of non-pharmacologic interventions (Q6). Identified consequents as reinforcements included sedation effects from antipsychotic medications, ease of administering patient care, and the assurance of patient compliance with care.

2.4.1.4 Motivations & Goals

The researchers identified three constructs in the domain *Motivations & goals*: goal priority, goal/target setting, and implementation intervention. ICU and ward healthcare professionals defined several goal priorities to using antipsychotics including targeting achievement of patient and staff safety, and management of acute hyperactive delirium and agitation. ICU healthcare professionals additionally described weaning sedation, re-establishing day-night routine, and patient comfort as goal priorities. When reflecting on the goals with using antipsychotics, ICU and ward healthcare professionals identified achieving sedation and patient compliance with care delivery as their main goals (Q7). Participants frequently reported attempting to use non-pharmacologic interventions first including family engagement as their primary interventions to prevent and manage delirium (Q8).

2.4.1.5 Memory, Attention & Decision Processes

The researchers identified two constructs in the domain *Memory, attention & decision processes*: decision-making and cognitive overload. Decision-making in both the ICU and hospital ward were influenced by patient-specific factors (e.g., severity of delirium and agitation,

patient comorbidities), patient care goals (e.g., quantitative and qualitative sedation targets, patient goals of care), and multidisciplinary team opinions regarding the need for antipsychotics. Cognitive overload was particularly experienced by ward nurses due to high clinical demands and priorities that influenced their recommendations for the use of antipsychotics. As one nurse stated, "...there are times where you're saying this is unsafe, and we need to like calm this patient down. But the threshold of what is unsafe is dependent on what else is going on in the unit."

2.4.1.6 Environmental Context & Resources

Six constructs were identified from the domain *Environmental context & resources*: salient events/critical incidents, environmental stressors, resources/material resources, organizational culture/climate, person x environment interactions, and barriers and facilitators. ICU healthcare professionals spoke to salient events related to adverse drug effects from antipsychotic prescribing. As one ICU nurse reported, "there was a recent patient who had the serotonin syndrome as a result of antipsychotic use. ...and will likely be institutionalized for the rest of his life." Despite the identification of severe consequences, organizational culture toward antipsychotic use remained unchanged. One nurse compared the ICU and ward culture stating, "in ICU, the general kind of cultural practices, they want calm patients. They're used to sleeping patients or sedated patients. ...whereas on the trauma unit I used to work on, it was pretty normal to have two or three rangy patients that were trying to crawl out of bed for the entire shift." One physician spoke to the "institutional inertia" within the ICU as culturally driving antipsychotic prescribing practices (Q9). Other organizational culture factors included acceptance of chemical and physical restraints, differences in care goals during night shifts (vs. day shifts), and other unit or healthcare centre prescribing practices. These factors were often reported in the context of available resources, most notably lack of available patient monitoring on the hospital ward and lack of staffing availability in both the ICU and on the hospital ward

(Q10). Environmental stressors that promoted antipsychotic prescribing included unit structure on the ward (e.g., multi-patient rooms, frequent noise) and in the ICU (e.g., lack of windows, lights on at night), patient isolation due to infection protection and control, and the intrusiveness of treatments and care provided in the ICU (Q11). Person x environment interactions played a role in antipsychotic prescribing as a result of patient delirium and agitation severity in both the ICU and on the hospital ward (Q12). Participants highlighted several environmental barriers to minimizing antipsychotic prescribing and engaging in deprescribing including barriers to use of non-pharmacologic management of delirium and agitation (e.g., time constraints), lack of decision-making support tools around antipsychotic prescribing or deprescribing in both the ICU and on the hospital ward, and insufficient communication at transitions of care regarding new medications for ward healthcare professionals. Healthcare professionals in the ICU and on the ward identified family presence and engagement and non-pharmacologic intervention professionals (i.e., geriatricians) as facilitators to antipsychotic deprescribing (Q13).

2.4.1.7 Beliefs About Consequences

Five constructs from the domain *Beliefs about consequences* were identified: beliefs, characteristics of outcome expectancies, outcome expectancies, consequents, and anticipated regrets. Participants held multiple beliefs around antipsychotics being important in providing patient safety, staff safety, and sleep. Participants in both the ICU and on the ward described contrasting beliefs regarding the efficacy and futility of non-pharmacologic interventions that were dependent on the severity of agitation or delirium (Q14). Few participants viewed that not providing an antipsychotic medication for patients with delirium was a missed delirium treatment opportunity (Q15). Characteristics of outcome expectancies identified antipsychotics being the preferred alternative pharmacologic therapy for delirium with one physician stating, “being afraid to prescribe an antipsychotic might not be the best approach, especially if you’re thinking about alternatives like benzos, which have their own set of side effects and things.”. ICU and ward

healthcare professionals identified tension between consequents and outcome expectancies. Although they asserted there was a risk of adverse drug effects related to antipsychotic use with additional potential impacts on healthcare system utilization (e.g., increased length of hospital stay, future use of healthcare), participants felt that not using antipsychotics to achieve sedation in patients with delirium or agitation exposed patients to delays in therapy delivery (e.g., mobilization), could add additional healthcare system utilization costs, and could cause family distress. Other healthcare professionals reported the contrary that antipsychotics were responsible for delays in therapy (e.g., neurological examinations) and participation in care (**Q16 & 17**). Antipsychotic use was associated with anticipated regret around adverse effects, lack of deprescribing practices, and ongoing unnecessary antipsychotic prescriptions (**Q18**).

2.4.2 Participant-Identified Deprescribing Strategies

Participants shared suggestions of antipsychotic deprescribing strategies to reduce the proportion of critically ill patients discharged from hospital with an ongoing unnecessary antipsychotic prescription. Most participants (n=15, 71%), suggested the use of a direct communication tool between prescribers at transitions of care in addition to commonly completed transfer summaries. For example, participants discussed inclusion of specific instructions within transfer summaries to identify high-risk medications, such as antipsychotics, and provided explicit instructions on discontinuation recommendations. Additional recommendations by participants (n=15, 71%) focused on antipsychotic prescribing accountability practices including force-function alerts to identify antipsychotics for review, and automatic stop dates (**Table 2.6**).

2.5 Discussion

In this multi-centre, qualitative study of 21 critical care and hospital ward physicians, nurses, and pharmacists, seven relevant TDF domains and their associated constructs were identified as impacting antipsychotic medication prescribing and deprescribing practices of healthcare professionals for adult patients with and following critical illness. These domains included: *Social/professional role & identity*; *Beliefs about capabilities*; *Reinforcement*; *Motivations & goals*; *Memory, attention & decision processes*; *Environmental context & resources*; and *Beliefs about consequences*. Participant-generated recommendations further identified antipsychotic deprescribing strategies to facilitate safe practice pattern changes in-hospital through direct communication tools between prescribers at transitions of care and strategies to ensure antipsychotic medication prescribing accountability.

Our data further suggest that antipsychotic medications are being prescribed for multiple indications besides delirium such as patient and staff safety, sleep management, and environmental factors such as staff availability and workload. Individual and group beliefs as well as organizational structures, processes, and resource constraints appear to play an important role in why antipsychotic medications are prescribed and continued throughout a critically ill patient's hospitalization. Our study highlights the lack of structured antipsychotic prescribing guidelines and deprescribing assessments at all transitions of care. These handovers of care may benefit from our identified antipsychotic deprescribing strategies as interventions to ensure antipsychotic medications are not continued inappropriately in patients who experience critical illness.

Few studies have attempted to implement antipsychotic deprescribing interventions among critically ill patients at transitions of care [23-25]. These studies have had variable

success in effectively and sustainably reducing the number of critically ill patients discharged from hospital with ongoing antipsychotic prescriptions utilizing education, hand-off tools and algorithms, and pharmacist-driven prescriptive deprescribing authority as interventions [23-25]. This may be due to a lack of evidence-based rationale for implementation strategies addressing factors influencing healthcare professional behaviours. Our findings suggest targeting the additional relevant behaviour change domains identified may be needed for more effective and sustainable clinical results. Our results suggest that knowledge translation interventions to modify or reduce ongoing antipsychotic prescriptions such as environmental restructuring through antipsychotic prescribing and deprescribing guidelines and regulations, as well as the utilization of incentivization techniques with feedback on prescribing behaviours may more effectively impact antipsychotic prescribing and deprescribing behaviours [26].

Our study has several strengths including the recruitment of a broad sample of multidisciplinary healthcare professionals providing a comprehensive understanding of antipsychotic prescribing and deprescribing practices across transitions of care for critically ill patients. Additionally, our results have theoretical generalizability given the use of a previously validated framework [18]. Saturation was achieved for all domains but not constructs for each healthcare professional role. Not all constructs reported were identified by all healthcare professional roles implying saturation was not achieved for all constructs as certain perceptions were likely unique to the experience of a particular healthcare professional role. Our study also has limitations. Due to current pandemic constraints, we used convenience and snowball sampling for participant recruitment with most participants working in academic medical centres. It is possible that this sampling technique may have missed perspectives from healthcare professionals in other hospital structures (i.e., regional or community) that may have important and unique perspectives related to antipsychotic medication prescribing. Lastly, interviews took

place during the current COVID-19 pandemic which may have impacted some of the responses offered by participants.

2.6 Conclusions

Critical care and ward healthcare professionals report their antipsychotic prescribing practices being rooted in maintaining patient and staff safety as a means of delivering appropriate clinical care in patients with delirium and agitation. Although well-intentioned, antipsychotic prescribing in critical care is haphazard and not guideline based. Future interventions to reduce antipsychotic prescribing and promote antipsychotic deprescribing at transitions of care should address the identified relevant domains.

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**Table 2.1 Consolidated Criteria for Reporting Qualitative Research (COREQ)
Checklist**

Domain 1: Research team and reflexivity		
<i>Personal Characteristics</i>		<i>Location in Manuscript, section (page number)</i>
Which author/s conducted the interview or focus group?	NJ	Title page
What were the researcher's credentials? E.g. PhD, MD	NJ (MD, MSc), KDK (PhD), ES (Bkin/Bcom), DJN (MD, MSc, PhD), ZI (MD), LDB (PharmD), JPL (PhD), KMF (PhD)	Title Page
What was their occupation at the time of the study?	NJ (Attending Physician), KDK (Research Associate), ES (Graduate Student), DJN (Attending Physician, Assistant Professor), ZI (Attending Physician, Associate Professor), LDB (Pharmacist, Assistant Professor), JPL (Assistant Professor), KMF (Associate Professor)	Not reported in manuscript
Was the researcher male or female?	Female: NJ, KDK, LDB, JPL, KMF Male: DJN, ZI	Not reported in manuscript
What experience or training did the researcher have?	All (training in qualitative methods, facilitator experience)	Methods (page 5-6)
<i>Relationship with participants</i>		
Was a relationship established prior to study commencement?	Yes	Methods (Page 5)
What did the participants know about the researcher? E.g. personal goals, reasons for doing the research	Participants received an email outlining the objectives of the study, verification of ethical approval, and an informed consent form detailing the interview process. An additional oral consent process was completed with all participants and an opportunity to ask and answer all questions occurred prior to commencement of the semi-structured interview.	Methods (Pages 5-6)
What characteristics were reported about the interviewer/facilitator? E.g., Bias, assumptions, reasons and interests in the research topic	Interviewer bias, participants aware of interviewer's interest in research topic	Methods (Pages 5-6)

Domain 2: Study design		
<i>Theoretical framework</i>		
What methodological orientation was stated to underpin the study? E.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	Deductive thematic analysis using the TDF	Methods (Page 6)
<i>Participant Selection</i>		
How were participants selected? E.g. purposive, convenience, consecutive, snowball	Convenience and snowball	Methods (Page 5)
How were participants approached? E.g. face-to-face, telephone, mail, email	Recruited via e-mail, social media	Methods (Page 5)
How many participants were in the study?	21	Results (Page 7)
How many people refused to participate or dropped out? Reasons?	Not applicable	Not applicable
<i>Setting</i>		
Where was the data collected? E.g. home, clinic, workplace	Virtually via Zoom	Methods (Page 5)
Was anyone else present besides the participants and researchers?	No	Methods (Page 5)
What are the important characteristics of the sample? E.g. demographic data, date	Demographic data	Table 2.3
<i>Data collection</i>		
Were questions, prompts, guides provided by the authors? Was it pilot tested?	Interview guides were provided to participants by the authors. All interview guides were pilot tested with an ICU RN, ICU physician, and ICU pharmacist.	Methods (Page 5), Appendix 2.1 and 2.2
Were repeat interviews carried out? If yes, how many?	No	Not reported in manuscript
Did the research use audio or visual recording to collect the data?	All semi-structured interviews were audio-recorded only using the audio recording feature on Zoom; participants were asked to turn off their cameras for the duration of the interview	Methods (Page 6)
Were field notes made during and/or after the interview or focus group?	Yes, but field notes were not utilized in the data analysis	Methods (Page 6)
What was the duration of the interviews or focus group?	All interviews lasted approximately 30 minutes to 1 hour	Methods (Page 6)
Was data saturation discussed?	Yes	Methods (Page 7)
Were transcripts returned to participants for comment and/or correction?	No. A personalized summary of the interview was sent to participants to review and	Methods (Page 6)

	provide comments and/or corrections	
Domain 3: analysis and findings		
<i>Data analysis</i>		
How many data coders coded the data?	Three (NJ, KDK, ES)	Methods (Page 6)
Did authors provide a description of the coding tree?	Yes	Methods (page 6, 7)
Were themes identified in advance or derived from the data?	Themes were identified in advance using the Theoretical Domains Framework	Methods (Page 6)
What software, if applicable, was used to manage the data?	Nvivo12	Methods (Page 6)
Did participants provide feedback on the findings?	A summary of the interview was returned to the participants for additional comments and/or corrections	Methods (Page 6)
<i>Reporting</i>		
Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? E.g., participant number	Yes. Quotations were presented by participant role	Results (Pages 7-14), Table 2.5
Was there consistency between the data presented and the findings?	Yes	Results (Pages 7-14), Tables 2.2 and 2.5
Were major themes clearly presented in the findings?	Yes	Results (Pages 7-14), Figure 2.1, Table 2.2
Is there a description of diverse cases or discussion of minor themes?	Yes	Results (Page 17)

Table 2.2 Relevant and Non-Relevant Domains, Constructs, and Beliefs Related to Antipsychotic Prescribing Practices Among Critical Care and Ward Healthcare Professionals Caring for Critically Ill Patients and Patients Following Critical Illness

Relevant Domains

Domains	Constructs	Beliefs
Social/professional role & identity	Professional confidence	- Prescription monitoring and safe prescribing practices (e.g., deprescribing ICU orders, prescribing for appropriate indications) - Self-identified knowledge gaps (e.g., know more about antipsychotics, knowledge about the patient)
	Professional identity/boundaries/role	- Perceived role in implementation of non-pharmacologic interventions - Patient advocacy - Healthcare professional boundaries between multidisciplinary team members
	Group identity	- Accepted prescribing practices - Collaboration in multidisciplinary environment - Interdepartmental and healthcare professional prescribing differences
Beliefs about capabilities	Professional competence	- Implementation of non-pharmacologic and pharmacologic interventions - Perceived deprescribing practices
	Perceived behavioural regulation	- Guideline adherence - Differential confidence in implementing prescribing recommendations
	Professional confidence	- Drug administration competency and appropriate monitoring - Antipsychotic management at transition of care - Night shift pharmacologic management
	Empowerment	- Individualized healthcare professional prescribing practices - Nurse requests for pharmacologic interventions
	Beliefs	- Acceptance of truth that antipsychotics useful for hyperactive delirium and agitation

		- Preferred safe sedation effects - Inefficacy of antipsychotics
Reinforcement	Consequents	- Sedation effects - Ease of patient care and patient compliance with care (e.g., less work, on-call calls)
	Incentives	- Patient and staff safety - Ease of pharmacologic administration - Agitation and delirium as routine event
	Reinforcements	- Patient volume and workload - Implementation and efficacy of non-pharmacologic interventions (e.g., failure of non-pharmacologic management in hyperactive delirium)
Motivation & goals	Goal priority	- Weaning sedation - Day-night routine - Patient and staff safety - Acute hyperactive delirium and agitation management - Comfort
	Goal/target setting	- Sedation - Patient compliance
	Implementation intervention	- Attempt to use non-pharmacologic interventions first - Family engagement
Memory, attention & decision processes	Decision making	- Patient specific factors (e.g., QTc, age, comorbidities, severity of delirium and agitation) - Multidisciplinary team opinions - Patient care goals (e.g., RASS, quantitative and qualitative assessments, weaning sedation) - Timing of deprescribing practices
	Cognitive overload	- Other clinical pressures and priorities
Environmental context & resources	Salient event/critical incidents	- Adverse effect events (e.g., severe long-term disability, death)
	Environmental stressors	- Unit specific considerations

		(e.g., sedation and agitation thresholds) - Unit physical structure (e.g., windows, multi-patient rooms, lights, noise) - Patient isolation - Intrusiveness of treatments provided in the ICU
	Resources/material resources	- Staffing availability - Availability of monitoring
	Organizational culture/climate	- Workplace culture around antipsychotic prescribing threshold - Chemical and physical restraints - Institutional inertia - Day vs night shift differences - Other healthcare centre and unit prescribing practices
	Person x environment interactions	- Patient environment interactions (i.e., delirium and agitation)
	Barriers & facilitators	- Barriers to non-pharmacologic management of delirium and agitation - Lack of decision-making support and policy/protocols - Communications at transitions of care
Beliefs about consequences	Outcome expectancies	- Sedation effects of antipsychotics - Delay in therapy delivery (e.g., diagnostics, mobilization) - Family distress
	Characteristics of outcome expectancies	- Antipsychotics preferred alternative therapy
	Anticipated regret	- Lack of deprescribing practices - Ongoing antipsychotic prescriptions without clinical indication - Adverse medication effects (e.g., oversedation)
	Consequents	- Risk of adverse effects - Impacts on healthcare system utilization (e.g., future use of healthcare, length of stay, increased cost)

	Beliefs	- Perception that patients should sleep at night - Effectiveness vs. futility of non-pharmacologic interventions, antipsychotics, and deprescribing practices - Patient and staff safety - Missed delirium treatment opportunity when not using antipsychotics
Non-relevant Domains		
<i>Domains</i>	<i>Constructs</i>	<i>Beliefs</i>
Knowledge	Knowledge about condition/scientific rationale	- Awareness of guidelines - Knowledge of pharmacologic effects (e.g., randomized control trials) - Knowledge of delirium bundle and non-pharmacologic interventions
Skills	Skills	- Applied knowledge (e.g., clinical experience, ability to identify etiologies of delirium) - Consistent identification of delirium and agitation
	Skill development	- Formal skill development (e.g., basic pharmacologic knowledge of drugs) - Informal skill development (e.g., clinical training programs)
	Ability	- Communication (i.e., between healthcare professionals and patients/families)
Optimism	Optimism	- Slow change to prescribing practices - Differential optimism (e.g., context dependent, optimism in deprescribing benefit) - Poor alternative therapeutic options
Intentions	Stability of intentions	- Influence of workplace and unit culture - Perceived responsible prescribing practices - Perceived deprescribing and de-intensifying practices at transition of care
	Stages of change model	- Awareness and use of delirium bundle

		- Pre-contemplation and indifference in antipsychotic prescribing behaviour regulation
Social influences	Social support	- Multidisciplinary approach to antipsychotic prescribing decisions
	Group identity	- Hierarchy of social influence between healthcare professionals - Belief in other healthcare professional knowledge - Family influence
	Group conformity	- Ingrained prescribing practices - Negotiations between healthcare professionals around antipsychotic prescribing - Multidisciplinary rounds and conversations to determine antipsychotic prescribing
	Social comparisons	- Individual prescriber practice patterns - Differential perceptions of antipsychotic efficacy between different healthcare groups (e.g., ICU vs. ward physicians)
	Group norms	- Professional boundaries and roles
Emotion	Burn-out	- Emotional and physical exhaustion with delirious and agitated patients
	Fear	- Worry about patient and staff safety
	Anxiety	- Anticipatory anxiety about availability of antipsychotics - Concern about ongoing antipsychotic prescribing at transitions of care
	Stress	- Frustration about limited available effective diagnostics and treatments for delirium - Frustration with multiple opinions and questions surrounding antipsychotic prescribing requests
	Affect	- Sense of futility with

		delirium management - Hopelessness around identifying effective treatment other than antipsychotics to treat delirium and agitation - Confusion (e.g., delirium research nebulous and changing frequently)
Behavioural regulation	Self-monitoring	- Antipsychotic de-escalation prescribing practices - Individual prescriber practices to regulate antipsychotic prescribing (e.g., review need for medications daily) - Intention to regulate antipsychotic prescribing behaviour
	Action planning	- Delirium discussion at rounds

Table 2.3 Participant Characteristics

Characteristic	Physicians (n=11)	Nurses (n=5)	Pharmacists (n=5)
Age category, years, n(%)			
20-29	0 (0%)	2 (40%)	0 (0%)
30-39	7 (64%)	3 (60%)	2 (40%)
40-49	3 (27%)	0 (0%)	2 (40%)
50-59	1 (9%)	0 (0%)	1 (20%)

≥60	0 (0%)	0 (0%)	0 (0%)
Sex, n(%)			
Female	5 (45%)	5 (100%)	3 (60%)
Work environment, n(%)*			
ICU	7 (64%)	3 (60%)	3 (60%)
Ward	4 (36%)	2 (40%)	2 (40%)
Academic	10 (91%)	5 (100%)	5 (100%)
Regional	1 (9%)	0 (0%)	0 (0%)
Work experience in role, years, n(%)			
0-5	9 (82%)	3 (60%)	1 (20%)
6-10	1 (9%)	2 (40%)	0
≥11	1 (9%)	0 (0%)	4 (80%)

*Three participants had current or previous roles in both the ICU and ward environment. Work environment identified as current role in which they ≥50% of their clinical time.

Table 2.4 The Theoretical Domains Framework Version 2 Adapted from Cane et al. [18]

Domains (definition)	Constructs
Knowledge <i>(an awareness of the existence of something)</i>	Knowledge (including knowledge of condition/scientific rationale) Procedural knowledge Knowledge of task environment
Skills <i>(an ability or proficiency acquired through practice)</i>	Skills Skills development Competence Ability

	Interpersonal skills Practice Skill assessment
Social/professional role and identity <i>(a coherent set of behaviours and displayed personal qualities of an individual in a social or work setting)</i>	Professional identity Professional role Social identity Identity Professional boundaries Professional confidence Group identity Leadership Organizational commitment
Beliefs about capabilities <i>(acceptance of the truth, reality or validity about an ability, talent or facility that a person can put to constructive use)</i>	Self-confidence Perceived competence Self-efficacy Perceived behavioural control Beliefs Self-esteem Empowerment Professional confidence
Optimism <i>(the confidence that things will happen for the best or that desired goals will be attained)</i>	Optimism Pessimism Unrealistic optimism Identity
Reinforcement <i>(increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus)</i>	Rewards (proximal/distal, valued/not valued, probable/improbable) Incentives Punishment Consequents Reinforcement Contingencies Sanctions
Intentions <i>(a conscious decision to perform a behaviour or a resolve to act in a certain way)</i>	Stability of intentions Stages of change model Transtheoretical model and stages of change
Motivation & goals <i>(mental representations of outcomes or end states that an individual wants to achieve)</i>	Goals (distal/proximal) Goal priority Goal/target setting Goals (autonomous/controlled) Action planning Implementation intention
Memory, attention & decision processes <i>(the ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives)</i>	Memory Attention Attention control Decision making Cognitive overload/tiredness
Environmental context & resources <i>(any circumstances of a person's situation or environment that discourages</i>	Environmental stressors Resources/material resources Organizational culture/climate

<i>or encourages the development of skills and abilities, independence, social competence and adaptive behaviour)</i>	Salient events/critical incidents Person x environment interaction Barriers and facilitators
Social influences (those interpersonal processes that can cause individuals to change their thoughts, feelings or behaviours)	Social pressure Social norms Group conformity Social comparisons Group norms Social support Power Intergroup conflict Alienation Group identity Modelling
Emotion (a complex reaction pattern, involving experiential, behavioural, and physiological elements, by which the individual attempts to deal with a personally significant matter or event)	Fear Anxiety Affect Stress Depression Positive/negative affect Burn-out
Behavioural regulation (anything aimed at managing or changing objectively observed or measured actions)	Self-monitoring Breaking habit Action planning
Beliefs about consequences (acceptance of the truth, reality, or validity about outcomes of a behaviour in a given situation)	Beliefs Outcome expectancies Characteristics of outcome expectancies Anticipated regret Consequents

Table 2.5 Exemplar Quotations for All Identified Domains and Constructs

Quotation Number (Number/Participant group)	Constructs	Exemplar quotation
<i>Social/professional role & identity</i>		
Quotation number 1 Nurse	Professional identity/boundaries/role	"I think your role as the nurse is to, yeah, to advocate for your patients. So for example, the last time I can think of asking one of my prescribers for Seroquel was, we had a patient who, he was

		getting a nightly dose of Seroquel to help with his agitation in the ICU, coming out of it. And he was extremely agitated, moving around, crawling out of bed. It was quite unsafe.”
Quotation number 2 Physician	Professional confidence	“We really only prescribe the medications with very specific disclaimers if we are going to use low-dose PRN antipsychotics, and usually we prescribe them kind of with a disclaimer which says something like, “This is only to be used for significant agitation or aggression which is putting the individual patient or others at risk of harm.””
<i>Beliefs about capabilities</i>		
Quotation number 3 Nurse	Beliefs	“I’m not convinced that antipsychotics really help with that in all instances”
Quotation number 4 Pharmacist	Perceived competence	“We’re all aware of some of the conflicting data out there, but I don’t know that they’re specifically following guidelines every time that they’re prescribing the antipsychotics”
Quotation number 5 Pharmacist	Perceived behavioural control	“I try and make a concerted effort to try and stop them before they leave the ICU, if we can, but that’s sometimes not even feasible from within, I would say like 50% of the patients”
Quotation number 6 Nurse	Empowerment/Professional confidence	“You can only talk to so many people, and get your message across when you’re working nights, versus when you’re working days and present for their rounds, and the whole team is there, and that sort of thing. I feel like you can make your message heard a lot more when you’re working on that shift versus working on other shifts,

		you've got to be a lot more creative with how you get your message across, when you're not there, when everybody else is there."
Reinforcement		
Quotation number 7 Physician	Incentives	"I think one of the things I would think of is what's the pre-test probability that this patient could cause harm to them or themselves if they're hyperactive delirium gets worse. So for instance, in a young traumatic brain injury patient who, say he's a young male who's strong and is needing four-point restraints, to prevent him from pulling out his ET tube or pulling out his line', then I think that's something I would probably lean more towards an early prescription of an antipsychotic to make sure that that doesn't happen."
Quotation number 8 Physician	Incentives	"In the ICU, unless the patient is exhibiting significant agitation that it's becoming a safety issue, it's important for me to try and not prescribe an antipsychotic, and especially once a patient's out of the ICU, my threshold becomes even higher to prescribe an antipsychotic"
Quotation number 9 Nurse	Reinforcement	"It becomes a point where, if you're on the floor and you have five other patients and you have a patient that's requiring one-to-one care because they're agitated, it's that kind of thing that you want to ensure that they're safe."
Quotation number 10 Physician	Reinforcement	"In terms of nursing, if you're using conservative strategies or non-pharmacologic strategies, it's a lot more work, reorienting people,

		potentially having to use restraints, bed alarms, noise”
<i>Motivations & goals</i>		
Quotation number 11 Physician	Goal/target setting	“So I guess the typical prescribing pattern for antipsychotics would be for, probably the three most common ones I would use would be in decreasing frequency, quetiapine or Seroquel, Haldol or olanzapine, and those are typically...or when I use them, I typically use them for either agitated delirium for their antipsychotic benefit, or for either non-specific agitation and sedation, where I tend to use them for their sedating effects.”
Quotation number 12 Nurse	Implementation intervention	“I do value the non-pharmacological interventions over pharmacological interventions. I find myself, I rarely use a PRN antipsychotic if needed. Yeah, I guess on a personal level, I try for the non-pharmacological first”
<i>Memory, attention & decision processes</i>		
Quotation number 13 Nurse	Cognitive overload	“I would say, not officially, but unofficially, there are times where you’re saying this is unsafe, and we need to like calm this patient down. But the threshold of what is unsafe is dependent on what else is going on in the unit.”
<i>Environmental context & resources</i>		
Quotation number 14 Nurse	Salient events/critical incidents	“There was a recent patient who had the serotonin syndrome as a result of antipsychotic use. And yeah, he....very, very sick from it and will likely be institutionalized for the rest of his life. So there’s initially, the consequences come to mind. Just that with antipsychotic

		use, there is risks to the patient.”
Quotation number 15 Nurse	Organizational culture/climate	“...in ICU, the general kind of cultural practices, they want calm patients. They’re used to sleeping patients or sedated patients. And when there becomes more of a behavioural issue, I think sometimes that can be a challenge in the current, in this particular for ICU whereas on the trauma unit I used to you work on, it was pretty normal to have two or three rangy patients that were trying to crawl out of bed for the entire shift.”
Quotation number 16 Physician	Organizational culture/climate	“I think, there’s years and years of probably, in my opinion, overprescribing these medications in the intensive care unit. And so then, that builds the culture of, “Well, I’ve seen this for the last 15 or 20 years.” I think that, that’s a big barrier, that kind of institutional inertia.”
Quotation number 17 Physician	Resources/material resources	“...so specifically around workforce resource, so if there is a patient who’s agitated and is going to be a fall risk on the ward, or a patient in the ICU that may remove lines and you’re short on staff or nursing to monitor those things, then you’re more likely to prescribe an antipsychotic, so the patient is quote, unquote, more safe.”
Quotation number 18 Physician	Environmental stressors	“It’s an interaction between the patient, the environment, and the caregivers. And the caregivers being whether that’s family, healthcare providers, whatever. And so the environment, the amount of times that you see patients become agitated at 3 PM

		which is shift change is frequent, because it is loud, because there is less people down the hallway.”
Quotation number 19 Pharmacist	Person x environment interactions	“It can be a challenge from time to time, if you have a very busy unit and you have several nurses that are doubled. If they’re doubled with a delirious patient and they’re taking care of their other patients, they might like... Or I don’t want to say like but they might request more pharmacologic management, especially if they’re at risk of pulling out tubes and lines and things, because they still have a second patient to look after and they don’t have time to be right at the bedside monitoring that delirious patient all the time.”
Quotation number 20 Nurse	Facilitators and barriers	“And that actually one thing, another thing too, I haven’t mentioned too for the other pieces that you’ve asked about, is sometimes if you have family available, then antipsychotic use is definitely going to go down. If you have family who are able to be at the bedside, who are able to reorient patients and have that connection, There’s absolutely less use of antipsychotics I would say, because you have someone that can sit at their bedside and who knows them, and who has that rapport with the patient.”
Beliefs about consequences		
Quotation number 21 Nurse	Beliefs	“Some people are better at encouraging ‘other’ options for managing patient agitation or sleep than others. I’ve known some really great and creative nurses/HCAs who

		will play music, sit at patient bedsides, or unit clerks who are happy to keep an eye on patients in chairs, chat with them or while patients colour at the desk or are given a 'job' of prepping/ripping labels or 'folding laundry', to keep hands busy and out of trouble. These only really work for mild to moderate agitation though, someone who is freaking out doesn't care about crayons. Orders for "therapeutic touch and massage" or "provide warm milk" come across patronizing and are generally not well received by nursing staff"
Quotation number 22 Physician	Beliefs	"If it seems "like, "Okay, they got a little bit better," then we keep going, and if we prescribed it and they got worse, I think there's an element of us having to feel like, "Okay, should we increase the dose, and should we try a different medication" We're a bit committed, I think. So, but those are all kind of things that I think more fall under the category of facilitators and barriers...I think missed delirium treatment opportunities is the big issue."
Quotation number 23 Physician	Characteristics of outcome expectancies	"Being afraid to prescribe an antipsychotic might not be the best approach, especially 'f you're thinking about alternatives like benzos, which have their own set of side effects and things...And it would be advantageous to still consider it."
Quotation number 24 Physician	Outcome expectancies	"You're reducing the risk of venous thromboembolic disease, aspiration, pneumonia, falls, fractures,

		delirium, all the things. Because I think often the antipsychotics just mask the issue as well."
Quotation number 25 Pharmacist	Consequents	"In not giving the medication to patients who are extremely agitated, the risk of them pulling IVs, falling out of bed, causing self-harm, harm to other patients, harm to staff if they lash out. And then again, in not giving the medication, then you're going to have to let's say, if a nurse is having difficulty with a patient, then she has to call in a colleague because it might take two of them to get the patient up."
Quotation number 26 Pharmacist	Anticipated regret	"I'm always concerned about the risk of them going home on this medication when they leave the ICU and go to the ward, and it's not clear in the transfer summary that this was supposed to be a temporary measure that should be titrated off before they go home. And then they end up being on it at home because the family doctor "aid, "Well, it was prescribed in hospital, they must need it. I guess I'll continue it.""

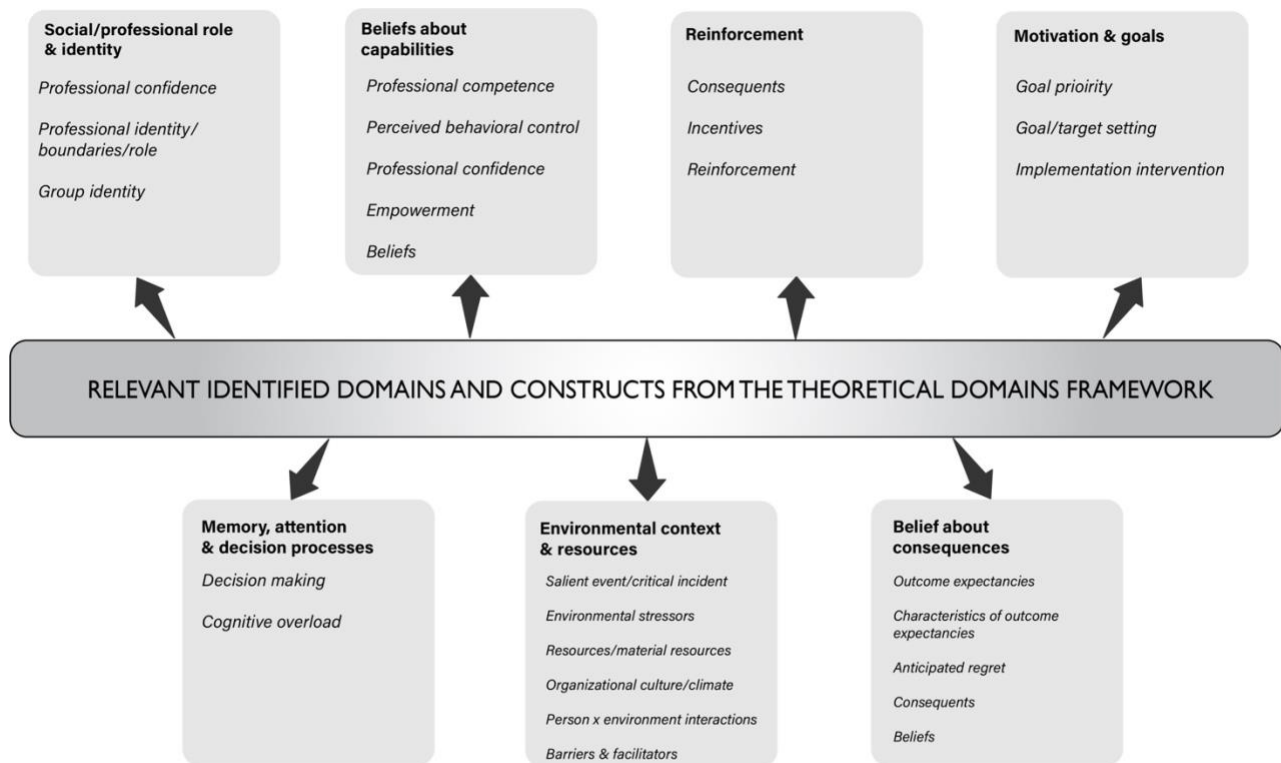
Table 2.6 Participant Identified Deprescribing Strategies

Deprescribing strategy	Participants reporting on strategy, (%)*
Direct communication tool between prescribers at transitions of care	15 (71%)
Antipsychotic medication prescribing accountability (e.g., automatic stop dates, no as needed dosing)	15 (71%)
Additional medication reconciliation at transitions of care	10 (48%)
Formal education sessions on indications for	9 (43%)

antipsychotic medication prescribing and deprescribing	
Expert consultations on medication management upon transition of care (e.g., geriatrics consultation, outpatient follow-up)	4 (19%)
Pharmacist-driven deprescribing strategies or algorithms	4 (19%)
Tapering protocols and discharge medication care bundles	4 (19%)
Antipsychotic prescribing policy development	1 (5%)
Practice audits	1 (5%)

* Percentages do not add up to 100 due to the possibility of multiple reported strategies per participant

Figure 2.1 Relevant Domains and Constructs According to the Theoretical Domains Framework in Relation to Antipsychotic Prescribing Practices Among Critical Care and Ward Healthcare Professionals Caring for Critically Ill Patients and Patients Following Critical Illness



Appendix 2.1 Physician Interview Guide



Facilitators and barriers to deprescribing antipsychotic medications in critically ill adult patients at transitions of care: A mixed methods study

Interview Guide

Introduction:

Thank you for agreeing to speak with me today about antipsychotic medication prescribing and deprescribing in patients with critical illness and following critical illness. We are conducting interviews with ICU and ward physicians, nurses and pharmacists across Alberta. We look forward to hearing about your experiences and expert knowledge. These topics serve as a guide only. If there are other details that you would like to share, I would like to hear them.

You were emailed a copy of the informed consent form. The consent form is part of the process of informed consent. It should give you an idea of what this research is about and your role as a participant.

Did you receive the consent form and have a chance to read it?

Because it is important that you understand your rights as a participant, we will review the main components of the consent form here.

[Read/review oral consent form]

Before we start, I would like to remind you that we will be audio recording this interview so that we can accurately capture our conversation. Do you agree to be audio recorded for research purposes?

I will start audio recording now. [Start audio recording]

Can you please verbally state that you consent to participate in this study?

Antipsychotic medications such as quetiapine and haloperidol are commonly prescribed to adult patients in the intensive care unit with non-psychiatric diagnoses. These medications are frequently continued at transitions of care in critically ill adult patients. Today we will be talking about your experience with prescribing and deprescribing antipsychotic medications in critically ill patients while in the ICU, following their transfer to the ward, and to hospital discharge. In 2018, the Society of Critical Care Medicine published Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in adult patients in the ICU.

Knowledge

1. Are you aware of current clinical practice guidelines for antipsychotic medication use in critically ill patients?

2. What is your understanding of clinical practice guidelines for antipsychotic medication use in critically ill patients?
3. Do you or does your unit use any parts of this guideline when prescribing antipsychotic medications to patients in the ICU or those patients transferred from the ICU?

Social/Professional role and identity

4. Does your role as a physician influence how you prescribe antipsychotic medications for critically ill patients or those patients that have experienced critical illness? How so?
(Prompt: For example, have you previously been trained to prescribe antipsychotics? Is this standard of practice? Is this an accepted prescribing practice in your unit?)

Social influences

5. Are there other healthcare providers that would influence whether or not you prescribe antipsychotics to critically ill patients or those patients who have been critically ill?
(Prompt: If so, who would that be and in what circumstance would that influence your behaviours?)

Behavioural regulation

6. Are there any policies or procedures in place that provide guidance on antipsychotic medication prescribing in the ICU or on the ward?
7. If you were going to not prescribe an antipsychotic medication, how confident would you be that this could be carried out in your unit?

Skills

8. What skills or skill set are required for you to make a decision to prescribe an antipsychotic medication to a critically ill patient or a patient that has been recently critically ill?

Beliefs about capabilities

9. What problems or challenges might you expect to encounter if you were to manage a patient without an antipsychotic medication?
10. What aspects of patient care or the professional provision of care might help to overcome these problems or challenges?

Environmental context and resources

11. Are there ways that the clinical environment either in the ICU or on the ward affects the use of antipsychotic medications?
(Prompt: If so, how does the clinical environment affect the use of antipsychotic medications?)

Beliefs about consequences

12. What are the benefits of not prescribing a critically ill patient or a patient that has recently been critically ill antipsychotic medications?
(Prompts: to yourself, to the patient, to the healthcare system?)
13. What disadvantages are there in not prescribing antipsychotic medications to a critically ill patient or a patient that has recently been critically ill?

(Prompts: to yourself, to the patient, to the healthcare system?)

14. Are there incentives in the ICU or on the ward to not prescribe patients antipsychotic medications?

Motivations and goals

15. How important is it to you that you do not prescribe antipsychotic medications to critically ill patients or those who have recently been critically ill?

Memory, attention, and decision processes

16. What factors might play a role in your decision-making process when deciding to prescribe antipsychotic medications to critically ill patients or those patients who have been recently critically ill?
17. In what situations would you find it difficult to use alternative interventions (i.e., non-pharmacologic or pharmacologic) other than antipsychotic medications in managing critically ill patients or those who have been recently critically ill?

Emotion

18. Are there any situations that you would have feelings of worry about not prescribing an antipsychotic medication?

Intentions

19. To what extent in your daily clinical practice do you intentionally regulate your prescribing of antipsychotic medications?

Optimism

20. How confident are you that reducing antipsychotic prescribing will improve patient care in the future?
(Prompt: Are you optimistic, pessimistic, or indifferent?)

Reinforcement

21. Are there any rewards or consequences if antipsychotic medications are prescribed to critically ill patients or those patients who have recently been critically ill?
(Prompts: to yourself? To patients? To the healthcare system?)

Closing questions

22. What potential strategies or approaches could be used to prevent critically ill patients from being discharged from hospital with antipsychotic medications that do not have a clinical indication?
23. Do you have anything you would like to share on this topic that we haven't discussed today?

Thank you for participating in our study. I will stop recording now and will ask some demographic questions.

[Stop recording]

Appendix 2.2 Pharmacist and Nursing Interview Guide



Facilitators and barriers to deprescribing antipsychotic medications in critically ill adult patients at transitions of care: A mixed methods study

Interview Guide

Introduction:

Thank you for agreeing to speak with me today about antipsychotic medication prescribing and deprescribing in patients with critical illness and following critical illness. We are conducting interviews with ICU and ward physicians, nurses and pharmacists across Alberta. We look forward to hearing about your experiences and expert knowledge. These topics serve as a guide only. If there are other details that you would like to share, I would like to hear them.

You were emailed a copy of the informed consent form. The consent form is part of the process of informed consent. It should give you an idea of what this research is about and your role as a participant.

Did you receive the consent form and have a chance to read it?

Because it is important that you understand your rights as a participant, we will review the main components of the consent form here.

[Read/review oral consent form]

Before we start, I would like to remind you that we will be audio recording this interview so that we can accurately capture our conversation. Do you agree to be audio recorded for research purposes?

I will start audio recording now. [Start audio recording]

Can you please verbally state that you consent to participate in this study?

Antipsychotic medications such as quetiapine and haloperidol are commonly prescribed to adult patients in the intensive care unit with non-psychiatric diagnoses. These medications are frequently continued at transitions of care in critically ill adult patients. Today we will be talking about your experience with prescribing and deprescribing antipsychotic medications in critically ill patients while in the ICU, following their transfer to the ward, and to hospital discharge. In 2018, the Society of Critical Care Medicine published Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in adult patients in the ICU.

Knowledge

1. Are you aware of current clinical practice guidelines for antipsychotic medication use in critically ill patients?
2. What is your understanding of clinical practice guidelines for antipsychotic medication use in critically ill patients?
3. Do you or does your unit use any parts of this guideline when prescribing antipsychotic medications to patients in the ICU or those patients transferred from the ICU?

Social/Professional role and identity

4. Does your role as a [pharmacist/nurse] influence how you recommend prescribing antipsychotic medications for critically ill patients or those patients that have experienced critical illness? How so?
(Prompt: For example, have you previously been trained to recommend prescribing antipsychotics? Is this standard of practice? Is this an accepted prescribing practice in your unit?)

Social influences

5. Are there other healthcare providers that would influence whether or not you recommend prescribing antipsychotics to critically ill patients or those patients who have been critically ill?
(Prompt: If so, who would that be and in what circumstance would that influence your behaviours?)

Behavioural regulation

6. Are there any policies or procedures in place that provide guidance on antipsychotic medication prescribing in the ICU or on the ward?
7. If you were going to recommend against prescribing an antipsychotic medication, how confident would you be that this could be carried out in your unit?

Skills

8. What skills or skill set are required for you to make a decision to recommend prescribing an antipsychotic medication to a critically ill patient or a patient that has been recently critically ill?

Beliefs about capabilities

9. What problems or challenges might you expect to encounter if you were to manage a patient without an antipsychotic medication?
10. What aspects of patient care or the professional provision of care might help to overcome these problems or challenges?

Environmental context and resources

11. Are there ways that the clinical environment either in the ICU or on the ward affects the use of antipsychotic medications?
(Prompt: If so, how does the clinical environment affect the use of antipsychotic medications?)

Beliefs about consequences

12. What are the benefits of not recommending prescribing a critically ill patient or a patient that has recently been critically ill antipsychotics medications?
(Prompts: to yourself, to the patient, to the healthcare system?)
13. What disadvantages are there in not recommending prescribing antipsychotic medications to a critically ill patient or a patient that has recently been critically ill?
(Prompts: to yourself, to the patient, to the healthcare system?)
14. Are there incentives in the ICU or on the ward to not recommend prescribing patients antipsychotic medications?

Motivations and goals

15. How important is it to you that you recommend against prescribing antipsychotic medications to critically ill patients or those who have recently been critically ill?

Memory, attention, and decision processes

16. What factors might play a role in your decision-making process when deciding to recommend prescribing antipsychotic medications to critically ill patients or those patients who have been recently critically ill?
17. In what situations would you find it difficult to use alternative interventions (i.e., non-pharmacologic or pharmacologic) other than antipsychotic medications in managing critically ill patients or those who have been recently critically ill?

Emotion

18. Are there any situations that you would have feelings of worry about not recommending the prescribing of an antipsychotic medication?

Intentions

19. To what extent in your daily clinical practice do you intentionally regulate your recommendations of prescribing antipsychotic medications?

Optimism

20. How confident are you that reducing antipsychotic prescribing will improve patient care in the future?
(Prompt: Are you optimistic, pessimistic, or indifferent?)

Reinforcement

21. Are there any rewards or consequences if antipsychotic medications are prescribed to critically ill patients or those patients who have recently been critically ill?
(Prompts: to yourself? To patients? To the healthcare system?)

Closing questions

22. What potential strategies or approaches could be used to prevent critically ill patients from being discharged from hospital with antipsychotic medications that do not have a clinical indication?
23. Do you have anything you would like to share on this topic that we haven't discussed today?

Thank you for participating in our study. I will stop recording now and will ask some demographic questions.

[Stop recording]

Appendix 2.3 Collected Participant Demographics Guide



Facilitators and barriers to deprescribing antipsychotic medications in critically ill adult patients at transitions of care: A mixed methods study

Post-interview demographic survey

Demographic Questions

We are collecting personal demographic information to describe our participants in aggregate. Any contact information you provide us will only be used to share a summary of our conversation here today if you would like to review it to ensure it reflects your thoughts. Please note that your demographic information and contact info will be stored in a password protected database that is only accessible to the study research team. If you are not comfortable answering any of the below questions you are welcome to skip any or all of those you do not wish to answer.

If applicable: What is the email address to which you wish to receive your transcription?

Demographics questions:

1. What is your age group?

- ☐ <20 years
- ☐ 20-29 years
- ☐ 30-39 years
- ☐ 40-49 years
- ☐ 50-59 years
- ☐ ≥60 years

2. What is your sex?

- ☐ Male
- ☐ Female
- ☐ Prefer not to answer

3. What is your current role?

- ☐ Nurse
- ☐ Nurse practitioner
- ☐ Resident
- ☐ Fellow
- ☐ Attending physician
- ☐ Pharmacist
- ☐ Other (please specify): _____

4. **[If applicable] What physician role do you identify as?**
- ☐ Primary clinician
 - ☐ Clinician scientist
 - ☐ Clinician educator
 - ☐ Clinician administrator
 - ☐ Other (please specify): _____
5. **How many years have you worked in your current role?**
- ☐ Please specify: _____
6. **How many years have you worked in critical care or within the hospital environment?**
- ☐ Please specify: _____
7. **What type of institution are you currently working in?**
- ☐ Academic
 - ☐ Non-academic
 - ☐ Regional
 - ☐ Urban
 - ☐ Other (please specify): _____
8. **How many beds in total does your hospital have?**
- ☐ ≤250
 - ☐ 251-499
 - ☐ 500-1000
 - ☐ >1000
 - ☐ Other (please specify): _____
9. **How big is the population your hospital serves?**
- ☐ Please specify: _____
10. **How many beds does your ICU or ward have?**
- ☐ Please specify: _____

**CHAPTER 3: A SCOPING REVIEW OF PERCEPTIONS OF HEALTHCARE
PROFESSIONALS ON ANTIPSYCHOTIC PRESCRIBING PRACTICES IN ACUTE
CARE SETTINGS**

Jaworska N., Moss SJ., Krewulak KD., Stelfox Z., Niven DJ., Ismail Z., Burry LD., Fiest KM. A scoping review of perceptions of healthcare professionals on antipsychotic prescribing practices in acute care settings. *Prepared for submission.*

3.1 Abstract

Background: Antipsychotic medications are frequently prescribed in acute care for clinical indications other than primary psychiatric disorders such as delirium. Unfortunately, they are commonly continued at hospital discharge and at follow-ups thereafter. The objective of this scoping review was to characterize antipsychotic medication prescribing practices, to describe healthcare professional perceptions on antipsychotic prescribing and deprescribing practices, and to report on antipsychotic deprescribing strategies within acute care.

Methods: We searched MEDLINE, EMBASE, PsycINFO, CINAHL, and Web of Science databases from inception date to July 3, 2021 for published primary research studies reporting on antipsychotic medication prescribing and deprescribing practices, and perceptions on those practices within acute care. We included all study designs excluding protocols, editorials, opinion pieces, and systematic or scoping reviews. Two reviewers screened and abstracted data independently and in duplicate. The protocol was registered on Open Science Framework prior to data abstraction ([10.17605/OSF.IO/W635Z](https://doi.org/10.17605/OSF.IO/W635Z)).

Results: Of 4528 studies screened, we included 80 studies. Healthcare professionals across all acute care settings (intensive care, inpatient, emergency department) perceived prescribing haloperidol (n=36/36, 100%) most frequently, while measured prescribing practices reported common quetiapine prescribing (n=26/36, 76%). Indications for antipsychotic prescribing were delirium (n=48/69, 70%) and agitation (n=20/69, 29%). Quetiapine (n=18/18, 100%) was most frequently prescribed at hospital discharge. Three studies reported in-hospital antipsychotic deprescribing strategies focused on pharmacist-driven deprescribing authority, handoff tools, and educational sessions.

Conclusions: Perceived antipsychotic prescribing practices differed from measured prescribing practices in acute care settings. Few in-hospital deprescribing strategies were described.

Ongoing evaluation of antipsychotic deprescribing strategies are needed to evaluate their efficacy and risk.

3.2 Introduction

Antipsychotic medications, which are licensed for chronic psychiatric disease management, are frequently prescribed in hospital for acute clinical indications such as delirium [1-4]. These medications do not appear to alter the incidence or duration of delirium despite a large body of high-quality evidence evaluating their clinical efficacy [2, 5-7]. An increasing understanding of the potential risk of oversedation, falls, metabolic effects and cardiovascular morbidity related to antipsychotic medication use in acutely ill patients has translated into current guidelines recommending against the routine prescribing of antipsychotic medications in these clinical contexts [5, 8-16]. Antipsychotic medication prescribing for non-traditional indications in the acute care setting remains common and has been demonstrated to lead to antipsychotic prescription continuation at hospital discharge [17-20].

In-hospital deprescribing strategies defined as the deliberate and supervised reduction or withdrawal of an inappropriate or unnecessary medication may be a tool to reduce the proportion of patients being discharged from hospital with ongoing antipsychotic medication where the clinical indication may no longer be appropriate [21, 22]. However, in-hospital deprescribing strategies are infrequently implemented [23]. In-hospital clinical environments provide a safe and monitored setting to facilitate the necessary steps required to initiate a deprescribing care plan and warrants further evaluation.

Defining antipsychotic medication prescribing practices and the perceptions surrounding antipsychotic medication use in the acute care setting is essential to developing effective,

sustainable, and collaborative multidisciplinary antipsychotic deprescribing strategies to promote appropriateness in prescribing and deprescribing during patient hospitalization [24-26]. The purpose of this scoping review is to synthesize the literature on antipsychotic medication prescribing practices in acute care, to describe healthcare professional perceptions on antipsychotic prescribing practices, and to report on antipsychotic deprescribing strategies within acute care.

3.3 Methods

The scoping review research questions and methods for study selection and data charting were developed using the methodology described by Arksey and O'Malley and the Scoping Review Methods Manual proposed by the Joanna Briggs Institute [27, 28]. The scoping review protocol was registered (Open Science Framework: [10.17605/OSF.IO/W635Z](https://osf.io/W635Z)), and submitted for open-access publication (*under review at BMJ Open*) prior to data abstraction. The review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis Extension for Scoping Reviews (PRISMA-ScR) checklist (**Appendix 3.1**) [29].

The scoping review aims to answer two research questions:

1. What prescribing practices do healthcare professionals utilize to guide prescribing and deprescribing of newly initiated antipsychotic medications in patients prescribed an antipsychotic for clinical indications other than a primary psychiatric diagnosis in acute care?
2. What perceptions, facilitators and/or barriers do healthcare professionals identify that influence the way antipsychotic medications are prescribed or deprescribed in acute care for patients with a clinical indication other than a primary psychiatric diagnosis?

The components of population, exposure, comparator, outcome, study design, and timeframe were defined. The population included adult patients (as defined in the primary study) admitted to any acute care setting excluding care centres associating with the acute care setting (e.g., rehabilitation units), and healthcare professionals (e.g., physicians, nurses, pharmacists). The exposure was defined as antipsychotic medication administration for clinical indications other than a primary psychiatric diagnosis (e.g., psychosis, schizophrenia, bipolar disorder, major depressive disorder), dementia, or cognitive dysfunction (e.g., developmental disorders). Antipsychotic medications included in the search strategy were haloperidol/Haldol®, quetiapine/Seroquel® (immediate release and extended release), risperidone/Risperdal® (immediate release and extended release), ziprasidone/Zeldox®/Geodon®, aripiprazole/Abilify®, olanzapine/Zyprexa®, and methotrimeprazine/Nozinan®. This list of medications was selected as they form the most common clinically used antipsychotic medications in acute care from clinical experience and from previous interventional and observational studies in the literature [18, 20, 30-32]. All comparators and comparisons were of interest. Outcomes of interest included antipsychotic medication prescribing practices (e.g., preferred antipsychotic prescribed, antipsychotic prescribed at hospital discharge, description of deprescribing initiatives) and perceptions of antipsychotic prescribing practices, (e.g., perceptions on knowledge, prescribing capabilities and consequences) for non-psychiatric diagnoses (e.g., exclusion of psychosis, schizophrenia, bipolar disorder, major depressive disorder), dementia, or cognitive dysfunction (e.g., developmental disorders). Any observational or experimental and quasi-experimental original primary research study was included. Unpublished abstracts and studies of original research (i.e., conference abstracts) were included. Protocols, editorials, opinion pieces, systematic or scoping reviews were excluded. All publications from database inception to July 3, 2021 were considered.

3.3.1 Data Sources and Searches

We systematically searched MEDLINE, EMBASE, PsycINFO, and CINAHL without restriction by date and language. Web of Science was searched for unpublished grey literature. The search strategy for MEDLINE was developed in consultation with a professional health sciences librarian (**Table 3.1**). All database searches were performed on July 3, 2021 using search terms that included subject headings, keywords, and associated synonyms reflecting antipsychotic prescribing and deprescribing practices, and perceptions of all healthcare professionals on antipsychotic medication prescribing and deprescribing within acute care. Search terms included the following keywords: antipsychotic medications (as defined by the pre-specified medication list), prescribing practices, acute care setting, and perspectives. A pre-specified list of antipsychotic medications (**Appendix 3.2**) was selected for this scoping review to maintain a clinically relevant focus on the most common antipsychotics prescribed in acute care from clinical experience and previous literature observational and interventional studies on antipsychotic medication prescribing [30-34]. Reference lists of identified studies were additionally searched for relevant studies.

3.3.2 Study Selection

Studies were selected that reported on either antipsychotic prescribing and deprescribing practices or perceptions in acute care. We defined antipsychotic prescribing or deprescribing practices in acute care as perceived (i.e., participant reported) or measured prescribing or deprescribing practices in patients who did not have a psychiatric diagnosis, dementia, or cognitive dysfunction (e.g., developmental disorders) where chronic antipsychotic medication use may be clinically indicated. We included studies for adult patients (as defined in the primary study) that were hospitalized at or presenting to an acute care facility (e.g., critically ill, medical, surgical ward patients, or emergency department) and all healthcare professionals

including, but not limited to physicians, nurses, and pharmacists. This study population was selected to reflect the population that is typically involved in the prescribing process of antipsychotic medications.

Studies identified through the bibliographic database search were first imported into Endnote-X9 (Clarivate, Philadelphia, USA) for de-duplication using the strategy outlined by Bramer *et al.* [35] and subsequently imported for title/abstract and full-text review into Covidence (Veritas Health Innovation, Melbourne, Australia). Two reviewers (NJ, ZS) screened titles/abstracts and full texts of studies independently and in duplicate for inclusion eligibility. Before each stage a calibration exercise was performed among reviewers to achieve >75% interrater agreement in study selection. Articles not available in English were translated using Google Translate, which has been reported as a reliable tool for translating documents for systematic reviews [36, 37]. Only those studies that satisfied all inclusion criteria were selected for data abstraction. Two reviewer agreement was required for studies to proceed on to data abstraction. Disagreements regarding study selection were resolved through discussion between the reviewers.

3.3.3 Data Abstraction

Two reviewers (NJ, SJM) completed a calibration exercise on ten studies to achieve >75% interrater agreement prior to data abstraction. Data were abstracted by two reviewers (NJ, SJM) independently and in duplicate using a standardized data abstraction form. We abstracted the following data: study identifiers and type (e.g., study location, study design, sample size, study setting), participants (e.g., healthcare professionals, patients), exposure (e.g., antipsychotic type, antipsychotic dosing), and outcome (e.g., perceived or measured antipsychotic prescribing practices, antipsychotic medication prescribed at hospital discharge,

antipsychotic knowledge and perceptions) as well as information on antipsychotic deprescribing approaches and strategies. We contacted corresponding authors via email once with no follow-up email for clarification if no specific antipsychotic medication was defined in the study.

3.3.4 Data Synthesis and Analysis

Studies were summarized following validated guidelines for narrative synthesis of quantitative studies [29, 38]. Considering heterogeneous quantitative data from included studies, we grouped studies according to outcomes and setting (i.e., intensive care, inpatient, emergency department) and summarized data as counts with proportions.

Studies describing perceptions of healthcare professionals on antipsychotic medication prescribing were evaluated for inclusion in deductive thematic qualitative analysis utilizing the TDF. The TDF is a theoretical framework of 14 behaviour and behaviour change domains and associated constructs that identifies pertinent factors that influence the behaviour patterns of healthcare professionals [38, 39]. Qualitative thematic analysis was performed to understand the reported priority factors that influence healthcare professional prescribing practices. We used a two-stage approach described by Braun & Clarke to evaluate included studies [40]. One reviewer (NJ) completed analysis for all included studies with second reviewer (SJM) verifying the data for accuracy. In the first stage, text from included studies was read line-by-line to identify and categorize specific codes to the TDF domains [40]. In the second stage, text was analyzed for discrete TDF constructs within each domain [38]. Disagreements in coding of text to a domain or construct were resolved through discussion between the two reviewers. All studies for qualitative analysis were in English and did not require translation.

3.4 Results

We identified 4,528 unique studies, of which 218 full texts were reviewed and 65 studies were included. An additional 49 studies were identified from reference searching, of which an additional 15 studies were included totalling 80 eligible studies (**Appendix 3.3**). Most studies were excluded as they did not report on a specific antipsychotic medication (n=33/153, 22%) (**Figure 3.1**).

3.4.1 Description of Studies

Studies were conducted between 1996 to 2021 (inclusive) with most studies being carried out between 2016 to 2018 (**Figure 3.2**). Most studies were conducted in North America (n=42/80, 53%), Europe (n=16/80, 20%), or Asia (n=8/80, 10%) and evaluated the intensive care (n=49/80, 61%), inpatient non-intensive care setting (n=27/80, 34%) or emergency department setting (n=5/80, 6%) (**Figure 3.3**). One study reported on both the intensive care and inpatient setting. Studies included healthcare professionals (n=36/80, 45%), patients (n=42/80, 53%), or both healthcare professionals and patients (n=2/80, 3%). All studies describing perceptions on antipsychotic medication prescribing were comprised of healthcare professionals, namely physicians (including physician assistants and nurse practitioners), nurses, pharmacists, and respiratory therapists. Study characteristics are listed in **Table 3.2**.

3.4.2 Antipsychotic Prescribing Practices Across Acute Care Settings

Of the included studies in the intensive care setting (n=49/80, 61%), most described participant-reported prescribing practices (intensive care, n=24/49, 49%; inpatient, n=8/27, 30%; emergency department, n=4/5, 80%), measured (i.e., actual) prescribing practices (intensive care, n=16/49, 33%; inpatient, n=14/27, 52%), or characterized the monitoring and management

of pain, agitation, or delirium (intensive care, n=19/49, 39%; inpatient, n=1/27, 4%) (**Table 3.3; Table 3.4**).

Most studies (n=69/80, 86%) described the antipsychotic prescribing indication. In the intensive care and inpatient setting, antipsychotic prescribing indications were delirium (intensive care, n=34/43, 79%; inpatient, n=14/21, 67%) or agitation (intensive care, n=9/43, 21%; inpatient, n=7/21, 33%). Agitation was the most common antipsychotic prescribing indication in the emergency department (n=4/5, 75%) (**Table 3.5; Table 3.6**). In all three settings, haloperidol was perceived to be the most common prescribed antipsychotic medication in studies describing healthcare professional-reported antipsychotic prescribing practices (intensive care, n=24/24, 100%; inpatient, n=8/8, 100%; emergency department, n=4/4, 100%) (**Table 3.6; Table 3.7**).

Evaluation of measured antipsychotic prescribing practices identified 34 studies (intensive care, n=20/34, 59%; inpatient n=14/34, 42%; emergency department n=0/34, 0%). In both the intensive care and inpatient setting, haloperidol remained a commonly prescribed antipsychotic medication (intensive care, n=14/20, 70%; inpatient, n=12/14, 86%). In the intensive care and inpatient setting, quetiapine (intensive care, n=17/20, 85%; inpatient, n=9/14, 85%), olanzapine (intensive care, n=14/20, 70%; inpatient, n=9/14, 70%), and risperidone (intensive care, n=13/22, 65%; inpatient, n=9/14, 65%) were also commonly prescribed (**Table 3.6; Table 3.8**). Co-prescription of sedative hypnotic medications in addition to antipsychotic medications included benzodiazepines (intensive care, n=24/28, 86%; inpatient, n=8/15, 53%), intravenous sedation infusions such as propofol or ketamine infusions (intensive care, n=9/28, 32%), and other additional antipsychotics (inpatient, n=8/15, 53%) (**Table 3.9; Table 3.10**).

Figure 3.4 illustrates studies reporting on measured antipsychotic medications prescribed at hospital discharge by setting and antipsychotic medication type. In both the intensive care and

inpatient setting, quetiapine was reported in all studies to be most often continued at hospital discharge (intensive care, n=12/12, 100%; inpatient, n=6/6, 100%). No studies were identified reporting on antipsychotic prescribing at hospital discharge in the emergency room setting.

3.4.3 Perceptions on Antipsychotic Prescribing Practices

The perceptions of healthcare professionals on antipsychotic medication prescribing practices from 29 included studies (n=29/80, 36%) were organized according to the domains of the TDF and by setting (**Table 3.11**). Most included studies describe perceptions in the ICU (n=18/29, 62%). Perceptions across all three settings were related to knowledge (e.g., knowledge of conditions requiring antipsychotics) (n=23/29, 79%), beliefs about capabilities (e.g., perceived competence regarding antipsychotic prescribing contexts such as delirium) (n=25/29, 86%), beliefs about consequences (e.g., beliefs surrounding antipsychotic efficacy for delirium) (n=23/29, 79%), and environmental context and resources (e.g., screening tools and protocols to guide antipsychotic prescribing) (n=21/29, 72%). **Figure 3.5** shows the perceptions of physicians (intensive care, n=13; inpatient, n=4; emergency department, n=4), nurses (intensive care, n=10; inpatient, n=1), pharmacists (intensive care, n=6; inpatient, n=1), and respiratory therapists (intensive care, n=1) according to the TDF. Some studies included aggregate responses from multiple healthcare professional roles (intensive care, n=6; inpatient, n=2). Four studies did not report on a healthcare professional role. Additional individual study thematic analysis delineating TDF domains and constructs is available in **Table 3.12**.

3.4.4 In-hospital Antipsychotic Deprescribing Strategies

Three (n=3/80, 4%) studies described antipsychotic medication deprescribing strategies in the acute care settings (**Table 3.13**). Two studies described a pharmacist-based intervention either in the form of an electronic handoff tool or the use of prescriptive authority to deprescribe

antipsychotic medications once the acute clinical indication had resolved. One study described the use of an antipsychotic discontinuation algorithm implemented prior to transfer out of the ICU. Two of the studies additionally described the use of education (pharmacist and multidisciplinary) regarding consensus guidelines on antipsychotic medication use in intensive care.

3.5 Discussion

We synthesized the evidence evaluating antipsychotic prescribing practices and the perceptions of healthcare professionals that influence the way this class of medications are prescribed for non-psychiatric diagnoses in acute care. Delirium and agitation were reported as the most frequent indications for antipsychotic prescribing. Across all acute care settings haloperidol was perceived as the most frequently utilized antipsychotic. In contrast, within the ICU and inpatient care settings actual antipsychotic prescribing practices identified prevalent use of atypical antipsychotics with quetiapine being the most frequently prescribed antipsychotic medication. Perceived antipsychotic prescribing practices differed from actual measured antipsychotic prescribing practices and may impact how antipsychotic medications are prescribed at hospital discharge. In both the ICU and inpatient settings, we found that quetiapine was the most frequently prescribed antipsychotic medication at hospital discharge and more accurately reflected measured actual antipsychotic prescribing practices than perceived antipsychotic prescribing practices.

Our findings identifying differing perceived versus actual measured antipsychotic prescribing practices has not previously been described. An explanation for these differences was not identified in our scoping review. It is possible that established high-quality evidence describing the increased risk of cardiovascular mortality and neurologic complications related to

haloperidol use may play a role in the decreased measured utilization of haloperidol despite reported preferences for haloperidol [41-43]. Despite a growing body of evidence focused on the clinical efficacy of antipsychotic medication use in delirium in both in the inpatient and intensive care setting demonstrating limited efficacy in mediating the prevention or duration of delirium, healthcare professionals continue to report prescribing antipsychotic medications [5-7, 44]. The prevalent use of quetiapine and its ongoing prescription at hospital discharge may reflect a new repurposing of this antipsychotic for sleep management following the resolution of delirium or agitation given its histaminergic properties [45]. Further, in the ICU setting limited alternative sedation-sparing medications available for the management of the symptoms of agitation or delirium likely remains a common driver for quetiapine prescribing [2, 7, 8].

Our study expands on healthcare professional prescribing perceptions specific to antipsychotic medications. Healthcare professionals feel confident in their antipsychotic prescribing abilities and identify antipsychotics as an effective clinical tool that does not carry sufficient risk of adverse events to limit their prescribing. Further, environmental factors such as delirium screening tools and the lack of established antipsychotic prescribing protocols to support these screening tools appears to influence healthcare professional prescribing practices. Few current studies are available that address in-hospital deprescribing strategies to reduce ongoing antipsychotic medication prescribing at hospital discharge [46-48]. Studies reporting on deprescribing strategies have been limited to the intensive care setting focusing on education initiatives and algorithmic deprescribing pathways with variable efficacy in sustainably reducing antipsychotic medication prescribing at hospital discharge [46, 47]. The implications of these results suggest that an approach addressing individual prescribing practice beliefs as well as targeting established health system processes through protocolized pathways may be necessary to produce effective and sustainable reductions in antipsychotic medication prescriptions continued at hospital discharge [49].

Our study has multiple strengths and notable limitations. We utilized a broad and comprehensive search strategy of multiple databases without restrictions including a grey literature search. Despite a comprehensive and exhaustive search strategy of the literature, it is possible that some relevant studies may have been missed as we limited our list of antipsychotic medications selected for this scoping review to focus on the most clinically relevant antipsychotic medications prescribed within acute care identified in the current literature and known to be utilized from clinical experience [31-34]. Limiting the search strategy to this antipsychotic medication list aimed to ensure feasibility, minimize heterogeneity of the data, and emphasize clinical applicability. However, generalizability may be limited in clinical environments where other antipsychotic medications may be more frequently used (e.g., low health resource clinical environments) and the results may be applicable to only certain countries (e.g., specific antipsychotics approved for use in the country). Lastly, few studies were identified regarding the antipsychotic prescribing practices within the emergency department and limited conclusions can be drawn regarding antipsychotic prescribing practices in this clinical setting.

3.6 Conclusions

Perceived antipsychotic prescribing practices differed from actual measured antipsychotic prescribing practices in acute care with more frequent prescribing of atypical antipsychotic medications in-hospital and at hospital discharge. Deprescribing strategies were infrequently described in the literature. Further research is needed to understand the reasons for inconsistencies between perceived and actual antipsychotic prescribing to develop in-hospital antipsychotic deprescribing strategies and to evaluate their efficacy and risks in expediting the translation of best evidence practices into clinical implementation.

3.7 References

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Table 3.1 Search Strategy Used in MEDLINE

Search component	Search terms	
Antipsychotic medications	1	exp antipsychotic agents/
	2	(antipsychotic* or anti-psychotic* or neuroleptic* or psychotropic* or haldol or haloperidol or quetiapine or seroquel or risperidone or risperidal or olanzapine or zyprexa or methotrimeprazine or nozinan or ziprasidone or zeldox or geodon or aripiprazole or abilify).ti,ab,kf.
	3	or/1-2
Perspectives	4	exp attitude of health personnel/
	5	exp attitude to health/
	6	exp health knowledge, attitudes, practice/
	7	(knowledge adj2 attitude* adj2 perception*).ti,ab,kf.
	8	(knowledge adj2 attitude* adj2 practice*).ti,ab,kf.
	9	(attitude* or stance* or opinion* or insight* or percepti* or belie* or facilitator* or facilitat* or experience* or perspective* or barrier* or challeng*).ti,ab,kf.
	10	or/4-9
Acute care setting	11	exp critical illness/
	12	exp intensive care units/
	13	exp critical care/
	14	exp hospitalization/
	15	exp inpatients/
	16	exp hospitals/
	17	(critical care* or critical ill* or critically ill* or intensive care* or intensive care unit* or ICU* or inpatient* or hospitaliz* or admit* or admission* or hospital*).ti,ab,kf.
	18	or/11-17
Prescribing practices	19	exp Practice Patterns, Physicians/
	20	exp Drug Prescriptions/
	21	(deprescrib* or deprescrip* or de-prescrib* or de-prescrip* or discontinu* or dis-continu* or deadopt* or de-adopt* or de-implement* or deimplement* or prescrib* or prescrip* or practic*).ti,ab,kf.
	22	(prescri* adj2 practice*).ti,ab,kf.
	23	(prescri* adj2 pattern*).ti,ab,kf.
	24	or/19-23
All	25	3 and 10 and 18 and 24

No limiters or restrictions were applied to any database searches.

Table 3.2 Characteristics of Included Studies

First author	Year	Research type	Study type	Country/Continent	Clinical specialty	Population	Number of included patients	Number of included healthcare professionals
Intensive Care								
Almehairi, E.	2018	Observational	Cross-sectional survey + chart review	United Kingdom	Intensive care	Patients and professionals	188	43
Boncyk, C.S.	2021	Observational	Retrospective cohort study	United States	Intensive care	Patients	7,879	
Brown, G.	1998	Interventional	Quasi-experimental study	Canada	Intensive care	Patients	78	
Collet, M.O.	2019	Observational	Focus groups	Denmark	Intensive care	Professionals		39
D'Angelo, R.G.	2019	Interventional	Pre-post interventional study	United States	Intensive care	Patients	281	
DeBacker, J.	2018	Observational	Retrospective cohort study	Canada	Intensive care	Patients	45	
Devlin, J.W.	2011	Observational	Cross-sectional survey	United States	Intensive care	Professionals		250
Dyal, S.	2019	Observational	Cross-sectional survey	United States	Intensive care	Professionals		94
Dzierba, A.L.	2019	Observational	Cross-sectional survey	United States	Intensive care	Professionals		221
Eastwood, G.M.	2012	Interventional	Quality improvement study	Australia	Intensive care	Professionals		174
Ely, E.W.	2004	Observational	Cross-sectional survey	United States	Intensive care	Professionals		912
Farrokh, S.	2017	Observational	Retrospective cohort study	United States	Intensive care	Patients	100	
Flores, D.J.	2015	Observational	Cross-sectional survey	United States	Intensive care	Professionals		41
Gilbert, B.	2017	Observational	Retrospective cohort study	United States	Intensive care	Patients	236	
Gill, K.V.	2012	Observational	Cross-sectional survey + retrospective cohort study	United States	Intensive care	Patients and professionals	496	53
Glass, M.	2018	Interventional	Pre-post interventional study	Not reported	Intensive care	Patients	100	
Johnson, K.	2016	Interventional	Pre-post interventional study	United States	Intensive care	Professionals		72
Kim, D.H.	2018	Observational	Retrospective cohort study	United States	Cardiac surgery	Patients	293,212	
Kloet, M.A.	2017	Interventional	Quality improvement study	United States	Intensive care	Patients	393	
Kram, B.L.	2015	Observational	Retrospective cohort study	United States	Intensive care	Patients	156	
Kram, B.L.	2019	Interventional	Quality improvement study	United States	Intensive care	Patients	358	

Levine, A.R.	2019	Observational	Retrospective cohort study	United States	Intensive care	Patients	279
Marshall, J.	2016	Observational	Retrospective cohort study	United States	Intensive care	Patients	39,246
Mo, Y.	2017	Observational	Cross-sectional survey	United States	Intensive care	Professionals	635
Palacios-Ceña, D.	2016	Observational	Focus groups	Spain	Intensive care	Professionals	38
Patel, M.	2019	Observational	Retrospective cohort study	Not reported	Intensive care	Patients	43
Patel, R.P.	2009	Observational	Cross-sectional survey	United States	Intensive care	Professionals	1,384
Ranzani, O.T.	2014	Interventional	Quality improvement study	Brazil	Intensive care	Patients	22,965
Rhoney, D.H.	2003	Observational	Cross-sectional survey	United States	Intensive care	Professionals	474
Silverman, D.	2013	Observational	Retrospective cohort study	United States	Intensive care	Patients	70
Stuart, M.M.	2020	Interventional	Quasi-experimental study (retrospective)	United States	Intensive care	Patients	158
Swan, J.T.	2012	Observational	Retrospective cohort study	United States	Intensive care	Patients	164,996
Thiboutot, Z.	2016	Observational	Prospective cohort study	Canada	Intensive care	Patients	712
Tomichak, J.E.	2016	Observational	Prospective cohort study	United States	Intensive care	Patients	500
Trogrlic, Z.	2013	Observational	Prospective cohort study	Netherlands	Intensive care	Patients	1,576
van den Boogaard, M.	2009	Interventional	Quality improvement study	Netherlands	Intensive care	Patients	1,742
Inpatient							
Al-Qadheeb, N.S.	2013	Observational	Prospective cohort study	United States	All acute care settings	Patients	180
Basciotta, M.	2018	Observational	Retrospective cohort study	United States	All acute care settings	Patients	150,948
Bascom, P.B.	2014	Observational	Case report or case series	USA	Palliative care	Patients	2
Bedouch, P.	2015	Observational	Cross-sectional survey	France	All acute care settings	Professionals	201
Birigen, E.K.	2021	Observational	Cross-sectional survey	United States	Oncology	Professionals	65
Brennan, M.	2018	Observational	Case-control	USA	Geriatrics	Patients	1,570
Brett, J.	2020	Observational	Retrospective cohort study + chart review	Australia	Geriatrics	Patients	793
Briskman, I.	2010	Observational	Retrospective cohort study	Israel	All acute care settings	Patients	191
Costa-	2014	Observational	Retrospective cohort study	Portugal	All acute care	Patients	193

Dias, M.J.					settings		
Fontaine, G.V.	2018	Observational	Retrospective cohort study	United States	All acute care settings	Patients	8,297
Herzig, S.J.	2016	Observational	Retrospective cohort study	United States	All acute care settings	Patients	2,695,081
Hosie, A.	2021	Observational	Cross-sectional survey	Australia (All)	All acute care settings	Professionals	475
Hui, D.	2011	Observational	Retrospective cohort study	United States	Palliative care	Patients	100
Kuscu, M.K.	2004	Observational	Cross sectional survey + semi-structured interviews	Turkey	Internal medicine and surgery	Professionals	75
Loh, E.C.	2011	Observational	Case report or case series	Malaysia	Palliative care	Patients	3
Loh, K.P.	2016	Observational	Retrospective cohort study + chart review	United States	Internal medicine and surgery	Patients	260
Masman, A.D.	2015	Observational	Retrospective cohort study	Netherlands	Palliative care	Patients	208
Mattison, M.L.P.	2014	Interventional	Pre-post control interventional study	United States	All acute care settings	Patients	19,949
McNeill, R.	2021	Observational	Retrospective cohort study	New Zealand	Palliative care	Patients	50
Meagher, D.	2013	Observational	Cross-sectional survey	Europe [†]	All acute care settings	Professionals	200
Someya, T.	2001	Observational	Cross-sectional study	Japan	Psychiatry	Patients	167
Thacker, S.	1996	Observational	Cross-sectional survey	United Kingdom	All acute care settings	Professionals	46
Trenaman, S.C.	2018	Observational	Cross-sectional study	Canada	All acute care settings	Patients	585
Tropea, J.	2009	Observational	Medical record audit	Australia	All acute care settings	Patients	174
Weir, D.L.	2020	Observational	Prospective cohort study	Canada	Internal medicine, cardiac and thoracic surgery	Patients	2,402
Wong, A.	2014	Observational	Retrospective cohort study	Canada	All acute care settings	Patients	76
Yasuyuki, O.	2016	Observational	Cross-sectional survey	Japan	Psychiatry	Professionals	154
Emergency department							
Bervoets, C.	2015	Observational	Cross-sectional survey	Belgium	Emergency department	Professionals	110
Campillo, A.	2012	Observational	Retrospective cohort study	United States	Emergency department	Patients	1,253
Chan, E.W.	2011	Observational	Cross-sectional survey	Australia, New Zealand	Emergency department	Professionals	783
Chan, E.W.	2015	Observational	Cross-sectional survey	Hong Kong	Emergency department	Professionals	281
Cowling, M.	2019	Observational	Cross-sectional survey	United States	Emergency department	Professionals	129

Organized in order of setting; author; then publication year

†United Kingdom, Netherlands, Italy, Switzerland, Germany, Spain, Portugal, Ireland, Sweden, Denmark, Austria

‡Argentina, Mexico, Chile, Colombia

Table 3.3 Measured or Reported Outcomes Evaluated on Antipsychotic Medication Prescribing Practices in Included Studies, by Acute Care Setting

MEASURED OR REPORTED OUTCOMES	ACUTE CARE SETTING		
	Intensive care ¹ N=49	Inpatient ¹ N=27	Emergency department N=5
Participant reported prescribing practices	24 (49%)	8 (30%)	4 (80%)
Measured prescribing practices	16 (33%)	14 (52%)	0 (0%)
Characterize monitoring and management of pain, agitation, or delirium	19 (39%)	1 (4%)	0 (0%)
Measured prescribing practices at transitions of care	9 (18%)	3 (11%)	0 (0%)
Antipsychotic deprescribing	3 (6%)	0 (0%)	0 (0%)
Evaluation of Inappropriate antipsychotic prescribing practices	1 (2%)	2 (7%)	0 (0%)
Delirium outcomes ²	2 (4%)	1 (4%)	0 (0%)
Mortality	2 (4%)	1 (4%)	0 (0%)
Sedation effects	1 (2%)	1 (4%)	1 (20%)
Prescribing practice audit	1 (2%)	0 (0%)	0 (0%)
Falls	0 (0%)	1 (4%)	0 (0%)

Percentages do not add up to 100 due to the possibility of multiple outcomes per study

¹One primary study reports combined outcomes for patients admitted as inpatients and in ICU and results reported in both categories

²Includes days-free of delirium and delirium resolution

Table 3.4 Antipsychotic Reported Outcomes of Included Studies

Intensive care															
First author	Year	Study type	Country/Continent	Reported or measured antipsychotic outcomes										Falls	Conclusions*
				Participant reported prescribing practices	Measured prescribing practices	Characterize monitoring and management of pain, agitation, or delirium	Measured prescribing practices at transitions of care	Antipsychotic deprescribing	Evaluation of inappropriate antipsychotic prescribing practices	Delirium outcomes	Mortality	Sedation effects	Prescribing practice audit		
Almehairi, E.	2018	Cross-sectional survey + chart review	United Kingdom										✓		Perceived versus actual prescribing practices may identify key areas for quality improvement. There were differences in the perceived and actual delirium assessment/plan and safety monitoring.
Boncyk, C.S.	2021	Retrospective cohort study	United States							✓	✓				Pharmacologic interventions, most often in the form of antipsychotic medications, for the treatment of ICU delirium are common, and often continued after delirium resolution and hospital discharge.
Brown, G.	1998	Quasi-experimental study	Canada									✓			With the implementation of a medication algorithm to promote sleep in the ICU with methotrimeprazine, there was no difference in the maximum number of continuous hours of sleep and additional sedating medications were required at night.
Ceraso, D.H.	2010	Cross-sectional survey	South America [†]	✓		✓									Despite considering delirium as a frequent, preventable problem and with serious repercussions for the critical patient, the intensivists surveyed did not use a tool for their evaluation or to guide antipsychotic medication prescribing in ICU. Efforts are necessary educational programs to disseminate the effectiveness and usefulness of the scales that early and accurate diagnosis of delirium in ICU.
Chawla, R.	2013	Cross-sectional survey	India	✓											Narcotics and non-narcotics are equally used analgesics. Haloperidol is the most common drug to treat delirium. Midazolam is the most commonly used sedative, but the current evidence driven use of fentanyl, propofol and dexmedetomidine is encouraging.
Collet, M.O.	2019	Focus groups	Denmark	✓											This study describes an algorithm of contemporary delirium management in Danish ICUs based on qualitative

															inquiry. When evidence-based solutions are unclear, nurses and physicians rely on personal experience, collective experience, and best available evidence to determine which patients to treat and what methods to use to treat ICU delirium. Delirium management still needs clear objectives and guidelines with evidence-based recommendations for first-line treatment and subsequent treatment options.
D'Angelo, R.G.	2019	Pre-post interventional study	United States		✓			✓							This is the first study to demonstrate a reduction in antipsychotic continuation at transition from the MICU after implementation of an antipsychotic discontinuation bundle in ICU patients. The authors believe this bundle allows for safer transitions of care from the MICU and decreases unnecessary antipsychotic therapy.
DeBacker, J.	2018	Retrospective cohort study	Canada		✓										Withdrawal from large doses of benzodiazepines and opioids administered over many days may play a role in the high incidence of delirium in patients on ECMO and warrants more investigation. If sedation minimization is achieved early after ECMO initiation, delirium and withdrawal syndromes may be reduced, thus allowing earlier and more aggressive mobilization.
Devlin, J.W.	2011	Cross-sectional survey	United States	✓											Practices and perceptions among the critical care pharmacists who responded to our survey regarding delirium recognition and treatment vary widely and are frequently not evidence-based. The survey findings may be related, in part, to the fact that there is a lack of rigorous evidence to guide many current ICU delirium recognition and treatment practices. While knowledge gaps surrounding ICU delirium recognition, prevention, and treatment among the pharmacists who responded to the survey are numerous, increased formal educational activities in this area should go a long way to improving pharmacists' knowledge and practice in this area.
Dyal, S.	2019	Cross-	United States	✓											Assessment and management

		sectional survey													strategies of acute severe alcohol withdrawal vary considerably. Benzodiazepines are the mainstay of treatment. Atypical antipsychotics, haloperidol, among other sedative medications were all found to be significantly more likely to be utilized for prevention of central nervous system depression.
Dzierba, A.L.	2019	Cross-sectional survey	United States	✓		✓									Most respondents use validated scales and protocols to assess and manage pain, agitation/sedation, and delirium. The majority of respondents reported targeting a deep level of sedation with propofol being used for both deep and light levels of sedation. Reported delirium prevention strategies for patients on VV-ECMO include scheduled antipsychotics and scheduled haloperidol. Delirium treatment strategies include scheduled haloperidol and as needed atypical antipsychotics.
Eastwood, G.M.	2012	Quality improvement study	Australia		✓										Critical care nurses in one Australian ICU who responded to our survey think delirium assessment is important. Although they find unstructured assessments easier to perform, they wanted to persist with the CAM-ICU, in part because it facilitated more appropriate pharmacological treatment of delirium for their patients. Twice as much olanzapine and nearly five times as much haloperidol was prescribed in the CAM-ICU period.
Ely, E.W.	2004	Cross-sectional survey	United States	✓											The results of this survey provide data that show an overall appreciation for delirium as an important form of organ dysfunction yet point to a general disconnect between the perceived importance of delirium in the ICU and current practices of delirium monitoring and treatment. Common treatments for delirium reported by respondents include predominantly haloperidol followed by atypical antipsychotics.
Farrokh, S.	2017	Retrospective cohort study	United States		✓		✓								Atypical antipsychotics initiated in the ICU were frequently continued after hospital discharge in our institution. Given the known risks associated with

															extended therapy, initiatives are needed to prevent inappropriate continuation beyond hospitalization.
Flores, D.J.	2015	Cross-sectional survey	United States	✓		✓									Education improved staff understanding of the clinical implications of patients with delirium and treatment.
Gilani, A.A.	2020	Cross-sectional survey	United Kingdom	✓		✓									There is great amount of variation in the treatment of delirium that may represent clinical experience and familiarity with agents and assessments, and the dearth of positive research results. Typical and atypical antipsychotics were commonly prescribed for delirium. Most practitioners reported de-escalating treatment after delirium resolved by gradual weaning of treatment over time.
Gilbert, B.	2017	Retrospective cohort study	United States		✓		✓								Continuation of neuroleptics initiated for acute illness in the ICU upon discharge from the unit and hospital is highly prevalent in line with evidence currently published in the literature. The risk of being discharged on these agents does not appear to be any more prevalent based on admitting service, admission diagnosis, requirement of MV, or even selection of sedative utilized. Instead, continuation of neuroleptics upon transitions of care appeared to be more prevalent among patients receiving sleep aids, those with negative urine drug screen, and those requiring initiation of multiple neuroleptics during ICU stay. These data support the need for a hospital protocol identifying patient populations susceptible to the inappropriate continuation of neuroleptics and facilitating their discontinuation, avoiding unnecessary adverse events and costs.
Gill, K.V.	2012	Cross-sectional survey + retrospective cohort study	United States	✓	✓										Haloperidol was the most commonly prescribed antipsychotic overall, primarily because of its high use on an as-needed basis. Of the patients receiving a scheduled (not as-needed) antipsychotic, quetiapine was used most often. For all ICU types, haloperidol was selected as the preferred drug for delirium. Observed differences between perceived and actual sedation practices, as

															well as the limited use of protocols, raise important questions regarding the challenges of the overall management of sedation in the US.
Glass, M.	2018	Pre-post interventional study	Not reported							✓					Medication assessment by pharmacists in patients screening positive for ICU delirium resulted in less haloperidol use.
Gong, Z.	2009	Cross-sectional survey	China	✓		✓									Delirium was believed to be a significant or serious problem and under-diagnosis was acknowledged by respondents. When asked what drugs should be used to treat delirium, respondents mentioned haloperidol and olanzapine. However, in their clinical practice, few doctors used these drugs to deal with the patient's delirium specifically. The vast majority of respondents had little knowledge on the diagnosis and the standard treatment of delirium.
Johnson, K.	2016	Pre-post interventional study	United States	✓		✓									An educational intervention emphasizing the importance of screening for delirium, risk factors for delirium and approaches to decrease the incidence of delirium can improve identifying and correctly treating delirium in a critical care setting. The two most frequent reasons cited for haloperidol pre-survey included minimal adverse side effects compared to lorazepam and less sedation. The two most frequent reasons cited for haloperidol post-questionnaire included less sedation and more effective than lorazepam with an increase in use of haloperidol.
Kim, D.H.	2018	Retrospective cohort study	United States		✓										In hospitalized older patients after cardiac surgery, we found that the rates of off-label antipsychotic medication use and potentially excessive dosing has declined, but substantial hospital-level variation and rapidly increasing trend in quetiapine use are concerning. To promote appropriate antipsychotic medication prescribing and improve clinical outcomes of older cardiac surgical patients, high-quality evidence on the effectiveness and harm of antipsychotics for management

															of delirium and training of health care providers about effective non-pharmacological interventions are urgently needed.
Kloet, M.A.	2017	Quality improvement study	United States						✓						In the ICU, antipsychotics were the most commonly encountered box warning drugs. These findings demonstrated the liberal use of antipsychotics that occurs in an ICU setting. Health care professionals should weigh the benefits of antipsychotic use against their risks, considering their questionable efficacy for ICU delirium
Kotfis, K.	2017	Cross-sectional survey	Poland	✓		✓									A majority of Polish ICUs do not adhere to international guidelines regarding sedation and delirium practices. High usage of benzodiazepines for sedation and ICU delirium treatment reveals persistence of non-evidence-based practice. Most frequently cited antipsychotic medications treat delirium were haloperidol followed by atypical antipsychotics.
Kram, B.L.	2015	Retrospective cohort study	United States				✓								Atypical antipsychotic prescribing in the ICU is associated with significant patient-centered implications, despite limited data supporting long-term benefit when initiated in this setting. Providers should assess the indication for atypical antipsychotics initiated in the ICU routinely and discontinue these medications before ICU transfer and hospital discharge appropriately to avoid prolonged and possibly unnecessary use.
Kram, B.L.	2019	Quality improvement study	United States				✓	✓							Implementation of a pharmacy-initiated electronic handoff tool may reduce the proportion of atypical antipsychotic-naïve ICU survivors with an atypical antipsychotic continued at the time of ICU transfer. The handoff tool was not associated with a significant reduction in the discharge prescribing rates of atypical antipsychotics for hospital survivors, but a clinically meaningful reduction was possibly achieved due to enhanced communication enabled by this tool.
Levine, A.R.	2019	Retrospective cohort study	United States					✓							A significant percentage of medical ICU and surgical ICU patients newly initiated on atypical antipsychotics remained

														on these agents at hospital discharge. Several risk factors influencing continuation of therapy existed in the two cohorts. Age >60 years, pre-existing dementia, hemorrhagic stroke, and initiation of risperidone were associated with continuation of antipsychotics at discharge in the medical ICU cohort. In the surgical ICU cohort, patients with TBI and those initiated on quetiapine were more likely to be discharged on antipsychotics. The high percentage of older patients and those with dementia prescribed atypical antipsychotics at discharge is concerning, given the known risks associated with long-term use in these patients. Implementation of strategies to prevent delirium and actively wean off antipsychotics once delirium has resolved may help reduce initiation and unnecessary continuation of these agents at hospital discharge.
Mac Sweeney, R.	2010	Cross-sectional survey	United Kingdom	✓		✓								UK consultant intensivists seem to recognise the significance of delirium in critically ill patients but despite this screening with validated tools is uncommon and hypoactive delirium is rarely treated. Haloperidol is the most common agent chosen to treat both hyper- and hypo-active delirium, in spite of concerns about side effects in non-ICU populations. This survey was undertaken to provide information on usual care of delirium in critically ill patients in the UK.
Marshall, J.	2016	Retrospective cohort study	United States					✓						The authors found that newly initiated antipsychotic therapy is a common occurrence in the ICU and that approximately one fifth of newly initiated patients are discharged from the hospital with these medications newly added to their medication lists in this single-center study. Perhaps even more concerning, we have identified that a patient's likelihood of continuing on these medications may not be entirely driven by the clinical needs of the patient but rather by nonclinical factors such as the type of

															antipsychotic used. Additional research is needed to better define the role of antipsychotic therapy post-critical illness and better delineate which patient populations would be suitable for continued treatment.
Mehta, S.	2007	Cross-sectional survey	Canada	✓											The results of this survey indicate that many ICU nurses are not content with current sedation and analgesia strategies and that most would welcome a strategy incorporating a protocol and a sedation scale. The most commonly reported antipsychotic used for sedation and analgesia in this survey was haloperidol.
Mo, Y.	2017	Cross-sectional survey	United States	✓		✓									This study demonstrates that ICU delirium practices have dramatically changed over the past decade. A majority of critical care practitioners were fully aware of the key components of the revised practice guidelines with regard to delirium management, such as delirium assessments and early mobilization. Respondents agreed that there is a need for well-conducted clinical trials to determine if haloperidol and atypical antipsychotics reduce the duration of delirium in adult ICU patients.
Palacios-Ceña, D.	2016	Focus groups	Spain	✓		✓									Our findings highlight how professionals perceive individuals with delirium. Doctors have difficulties selecting the appropriate drug, and for some patients, the dosage of the same is seen to vary across different shifts. Nurses believe that for the doctor, delirium is not a matter of urgency, and therefore the attention is often delayed. On the other hand, nurses have difficulty in applying verbal restraint, sleep management and early mobilisation, and there is a tendency towards the use of physical restraint while awaiting medical recommendations. The absence of a delirium protocol generates conflicts regarding which path of care to apply, especially during the night shift. The complexity of delirium itself, together with the associated therapeutic variety, and the presence of difficulties in the application of care, can lead to

															inappropriate patient management. These results may help to understand how doctors and nurses apply decision-making processes regarding delirium management. This study contributes to the evidence base suggesting that delirium in the ICU presents obstacles to management despite current existing guidelines.
Patel, M.	2019	Retrospective cohort study	Not reported		✓		✓								Pharmacologic sleep aids (including atypical antipsychotics) which are newly initiated in the ICU were commonly continued upon transfer out of the ICU.
Patel, R.P.	2009	Cross-sectional survey	United States	✓		✓									The results of this survey show discordance between the opinion that delirium is an important factor in patient outcome and the current practices in delirium monitoring and treatment. Although the number of people using a validated screening tool for delirium has increased significantly, this number is lower than expected. Most healthcare practitioners reported using a sedation protocol. Haloperidol was the most common medication reported for the treatment of delirium followed by atypical antipsychotics.
Ranzani, O.T.	2014	Quality improvement study	Brazil		✓	✓									The implementation of a light sedation policy is feasible in a group of nonteaching hospitals, and systematic monitoring of sedative consumption seems to be a simple and objective instrument for supporting the accomplishment of protocol on a large scale. The consumption of haloperidol showed no changes in the secular trend or postintervention; however, the consumption of haloperidol significantly increased immediately after intervention.
Rhoney, D.H.	2003	Cross-sectional survey	United States	✓											For sedative agents, morphine, lorazepam, haloperidol, and midazolam were used for longer than 72 hours by a majority of the respondents. 21% of the represented ICUs do not monitor sedation.
Salluh, J.I.F.	2009	Cross-sectional survey	Brazil	✓		✓									This survey provides valuable data on the perceived attitudes of Brazilian ICU physicians regarding sedation and delirium.

														Although delirium is acknowledged by most respondents as a severe medical condition, few systematic tools are used in clinical practice for the evaluation and treatment of delirium. Haloperidol and atypical antipsychotics were the most commonly reported antipsychotics used for delirium. The results of the present survey reemphasize the need to implement widespread educational efforts for the implementation of evidence-based strategies for the use of sedatives and the detection, monitoring, and treatment of delirium in ICU patients.
Selim, A.A.	2017	Cross-sectional survey	Egypt	✓		✓								Intensive care unit healthcare professionals do not have adequate training or routine screening of delirium. There is an evident absence of using standardised tools or adapting protocols to monitor and manage delirium. First-line treatment choices for delirium included sedatives and haloperidol.
Silverman, D.	2013	Retrospective cohort study	United States		✓	✓								Quetiapine administration may reduce benzodiazepine requirements and duration of restraint use. There is a high prevalence of continuation of quetiapine beyond the intensive care unit environment. This is a potential area for quality improvement with regards to medication reconciliation, limiting adverse effects, drug interactions, and cost. QTc interval should be monitored in patients receiving quetiapine.
Stuart, M.M.	2020	Quasi-experimental study (retrospective)	United States		✓		✓	✓						The implementation of a protocol for pharmacists with prescriptive authority to discontinue antipsychotics initiated for ICU delirium once ICU delirium resolves significantly decreases the rate of antipsychotic continuation at hospital discharge without increasing the recurrence of ICU delirium or QTc prolongation. This study demonstrated the impact of pharmacists assisting physicians in determining when antipsychotics can be discontinued to safely stop the medication prior to hospital discharge. Future studies are needed to assess antipsychotic

															discontinuation in the ICU setting, evaluate the need for tapering of antipsychotics, and determine the safety and efficacy of shorter duration taper protocols.
Swan, J.T.	2012	Retrospective cohort study	United States		✓										Antipsychotics are administered to 1 in every 10 ICU patients, and exposure to these medications is associated with increased ICU and hospital length of stay. Patients exposed to an antipsychotic, when there is no documentation of a mental disorder, have increased ICU length of stay, hospital length of stay and mortality compared to patients with documentation of a mental disorder. These findings do not support the use of antipsychotic medications in the ICU when patients do not have a documented diagnosis of a mental disorder or delirium. The appropriate indication and agent selection of the antipsychotics should continue to be studied in prospective, randomized, controlled trials. Due to the high prevalence of antipsychotic use in ICU patients who do not have a documented mental disorder, future studies are needed to describe the specific indications for antipsychotics and common doses that are being used in critically ill patients in current clinical practice.
Sztrymf, B.	2012	Cross-sectional survey	France	✓		✓									This study reports the findings of a French national survey on delirium screening and its management. Even though French ICU physicians participating in our survey are aware of the possible severity of delirium, they rarely use a dedicated and validated screening tool. Early patient mobilization is less frequent than declared as possible, mainly in mechanically ventilated patients. Treatments for delirium are reported to include antipsychotics, benzodiazepines, and hydroxyzine.
Thiboutot, Z.	2016	Prospective cohort study	Canada		✓										Delirium is increasingly associated with negative clinical outcomes, and recent guidelines have highlighted the importance of appropriate screening and modification of risk factors. This multicentre study identified

															infrequent use of delirium screening tools in Canadian ICUs. Antipsychotics were prescribed frequently, and patterns of use were variable. There is an opportunity to improve delirium screening and management of mechanically ventilated patients in Canadian ICUs.
Tomichek, J.E.	2016	Prospective cohort study	United States		✓		✓								In a large cohort of patients recovering from critical illness, antipsychotics were prescribed at hospital discharge to one out of every four patients newly treated with antipsychotics for delirium in the ICU, a practice most likely to occur among patients treated with an atypical antipsychotic in the hospital. Not only are the efficacy and safety of antipsychotics for delirium in the ICU unproven, but it remains unclear which antipsychotic, if any, should be used to treat delirium and for how long. Until clear evidence from large randomized trials is available regarding the efficacy and appropriate duration of antipsychotic use for delirium in the ICU, this class of medication should be used with caution. Focused efforts should be implemented to ensure antipsychotics are appropriately discontinued upon transitions of care in the hospital.
Trogrlic, Z.	2013	Cross-sectional survey	Netherlands	✓		✓									Our survey showed that healthcare professionals considered delirium an important but underdiagnosed form of organ failure. In contrast, screening tools for delirium are scarcely used, knowledge can be improved and protocolled treatment based on positive screening is often lacking. Haloperidol was the first-choice pharmacologic agents for the treatment of delirium. These results suggest that the focus of implementation of ICU delirium management should not be on motivational aspects, but on knowledge improvements, training in screening tools and implementation of treatment and prevention protocols.
Trogrlic, Z.	2013	Prospective cohort study	Netherlands		✓	✓									Daily screening for ICU delirium with a validated screening instrument is applied in less than

															one-half of the time in critically ill patients and management of delirium is often not guided by this screening. Haloperidol was used as the first-choice medication. Measures aimed at delirium prevention were carried only in a small minority. To implement protocolled delirium care in the region at study, a multifaceted tailored implementation program is needed.
van den Boogaard, M.	2009	Quality improvement study	Netherlands		✓										Tailoring an implementation strategy to the needs of the ICU was successful. The main goals were achieved within a relatively short time. Early recognition of delirium with the CAM-ICU has become a standard component of daily care by the nurses in the ICU and contributes to the quality of care. Early detection of delirium leads to lower dosage and shorter periods of haloperidol treatment in critically ill patients.
Wang, J.	2017	Cross-sectional survey	China	✓		✓									The practice of pain, agitation, and delirium assessment and management in China was in accordance with the international situations. The guideline and the updated recommendations were accepted by most of the clinicians in China. Haloperidol second most common medication used for delirium after dexmedetomidine.
Inpatient															
Al-Qadheeb, N.S.	2013	Prospective cohort study	United States		✓										Among long-term acute care hospital patients requiring permanent mechanical ventilation, scheduled antipsychotic therapy is used frequently and is associated with a greater incidence of psychiatric evaluation, delirium, as-needed antipsychotic use, and sitter use. Although scheduled antipsychotic therapy was used, related adverse effects are uncommon, and these effects are infrequently monitored
Basciotta, M.	2018	Retrospective cohort study	United States								✓				In hospitalized adults, typical antipsychotics may be associated with increased mortality or cardiopulmonary arrest, while atypical antipsychotics may only be associated with increased risk among adults age 65 and older.

Bascom, P.B.	2014	Case report or case series	USA									✓			Agitated delirium is a palliative care emergency. High doses of neuroleptic medications, with rotation to an alternate neuroleptic when side effects occur with standard haloperidol, may effectively palliate agitated delirium.
Bedouch, P.	2015	Cross-sectional survey	France	✓											The results of this large evaluation study of multiple medications including typical and atypical antipsychotics show that only a few types of drugs and errors constitute a substantial proportion of daily routine pharmacists' interventions. Various predictors of physicians' acceptance of pharmacist interventions are identified such as drug groups, intervention type, ward specialty and the degree of pharmacist on ward integration.
Birigen, E.K.	2021	Cross-sectional survey	United States	✓											Survey respondents indicated that formal education, medical literature, and input from palliative care and pharmacology colleagues informed their antipsychotic prescribing practices; a formal care pathway should integrate these different sources of information and provide specific resources in the community to help oncology providers connect their patients to long-term specialized psychiatric and therapeutic care.
Brennan, M.	2018	Case-control	USA		✓										Lower acute care of the elder (ACE) unit use of new antipsychotics may reflect better socialization, lower delirium rates, improved prescribing, early mobilization, skilled staff or an adjusted environment. The ACE team may have managed/prevented milder cases of agitation so that patients receiving antipsychotics were more distressed than their non-ACE peers.
Brett, J.	2020	Retrospective cohort study + chart review	Australia		✓										Off-label prescribing of quetiapine was common in this sample of inpatients, and senior hospital staff should remain cautious of quetiapine prescribing for indications where the evidence of harms and benefits remains unclear. Communication with community prescribers could also be improved to reduce the risk of conversion from intended short-

															term off-label use to longer-term use.
Briskman, I.	2010	Retrospective cohort study	Israel		✓										Risperidone may be the drug of choice for the treatment of delirium. However, due to the limitations inherent in a retrospective analysis and other methodological limitations, prospective large-scale trials are needed to support this recommendation.
Costa-Dias, M.J.	2014	Retrospective cohort study	Portugal											✓	Of the participants who took antipsychotic drugs, there was a seven times increased odds risk of fall and five times more risk of recurrent falls. The most common drug prescribed was haloperidol.
Fontaine, G.V.	2018	Retrospective cohort study	United States		✓		✓								Antipsychotics may be inappropriately continued in non-psychiatric patients at hospital discharge. Strategies to limit the number of potentially inappropriate antipsychotic prescriptions at hospital discharge should be evaluated to reduce the undue adverse effect burden and emergency department visits associated with antipsychotic use.
Herzig, S.J.	2016	Retrospective cohort study	United States		✓										in this large cohort of nonpsychiatric admissions to 300 US hospitals, antipsychotic medication exposure was common, often at high daily doses. Delirium and dementia were the strongest predictors of use among the patient and hospital characteristics examined. The variation in antipsychotic prescribing was not fully accounted for by measured patient characteristics and raises the possibility of differing hospital prescribing cultures.
Hosie, A.	2021	Cross-sectional survey	Australia (All)	✓											Clinicians' use of antipsychotic during delirium remains common and is primarily motivated by distress and safety concerns for the patient and others nearby. Delirium-related distress and safety concerns for patients, family, staff and others nearby are clinically meaningful and should be explicitly acknowledged and addressed in healthcare institutions and future studies.
Hui, D.	2011	Retrospective cohort study	United States		✓										In unselected advanced cancer patients with delirium in an acute palliative care unit, the median daily dose of neuroleptics was

															low, raising questions regarding the effectiveness of current neuroleptic use by palliative care specialists for management of delirium. Findings from this study highlight the need for prospective clinical trials to determine the safety, optimal dose, titration strategy and most appropriate combinations of neuroleptics for effective management of delirium symptoms, delirium recall and related distress.
Kuscu, M.K.	2004	Cross sectional survey + semi-structured interviews	Turkey	✓											Delirium remains an important clinical emergency in clinical practice. The evaluation of the attitudes of resident physicians toward delirium management including antipsychotic medication use will provide ground to develop new consensus guidelines for management of delirium.
Loh, E.C.	2011	Case report or case series	Malaysia							✓					Orodispersible olanzapine when used judiciously may have a useful role in managing refractory terminal delirium in palliative care setting and merits further study.
Loh, K.P.	2016	Retrospective cohort study + chart review	United States		✓		✓								Initiating an antipsychotic in the hospital is likely to result in long-term use of these medications despite associated antipsychotic risk of falls, fractures, stroke, cardiovascular disease, and increased mortality in those with underlying dementia. When possible, behavioural interventions to prevent delirium and slow the trajectory of decline should be implemented to reduce antipsychotic use.
Masman, A.D.	2015	Retrospective cohort study	Netherlands		✓										Haloperidol was commonly prescribed in combination with morphine and/or midazolam on day of death.
Mattison, M.L.P.	2014	Pre-post control interventional study	United States		✓										An intervention focused on delirium prevention and recognition by bedside staff combined with computerized decision support facilitates safer prescribing of high risk medications including antipsychotics, may results in less need for extended care.
McNeill, R.	2021	Retrospective cohort study	New Zealand						✓						This study compared the two deprescribing tools OncPal and STOPPFrail to an expert clinical review in an unselected palliative population. Haloperidol was the most common false positive drug identified for STOPPFrail.

Meagher, D.	2013	Cross-sectional survey	Europe [†]	✓		✓									Delirium awareness, delirium knowledge, and lack of education cited as most commonly reported barriers to improving the detection of delirium. Non-pharmacologic interventions were the first choice in hypoactive delirium and a combination of non-pharmacologic and pharmacologic interventions (using haloperidol and risperidone) were the first-line choice for delirium management.
Someya, T.	2001	Cross-sectional cohort study	Japan	✓											The present study discusses the results of a study on the use of medications for delirium, a condition commonly found in inpatients of general hospitals in Japan. Haloperidol was perceived as the first-line choice for the treatment of delirium. Due to fewer perceived side effects.
Thacker, S.	1996	Cross-sectional survey	United Kingdom	✓											This survey examines the prescribing opinions of junior doctors likely to be required to rapidly sedate an acutely agitated elderly patient. This study highlights the need for junior doctors to receive continuing education on the use of psychotropic drugs.
Trenaman, S.C.	2018	Cross-sectional cohort study	Canada		✓										There were no risk factors identified to predict continuation of an antipsychotic after a fall-related hospitalization. Prescribing quality may be assessed on a population level.
Tropea, J.	2009	Medical record audit	Australia		✓										This study provides valuable baseline information about what areas of practice are consistent with the guideline recommendations for the management of older people with severe symptoms of delirium and highlights which areas should be the focus for future quality improvement. In particular, commencing the antipsychotic agent at a low dose; and documentation of a clear management plan appear to be vital.
Weir, D.L.	2020	Prospective cohort study	Canada		✓		✓		✓						The incidence of potentially inappropriate medication prescribing (including antipsychotic medication prescribing) attributed to hospitalization is high, and this is associated with an increase in adverse drug events, emergency department visits.

															rehospitalizations, and death within 30 days of discharge.
Wong, A.	2014	Retrospective cohort study	Canada		✓										In the acute setting, psychiatrists and geriatricians may prescribe intramuscular olanzapine for behavioural symptoms in elderly patients. Commonly experienced adverse effects include lethargy, drowsiness, and constipation. Close monitoring is the key to ensuring safe use.
Yasuyuki, O.	2016	Cross-sectional survey	Japan	✓											There were areas of agreement and a lack of consensus regarding the first-line pharmacological treatment for delirium with a diverse range of clinical features. In the absence of a definitive treatment trial, most experts preferred to use risperidone or quetiapine for hyperactive delirium. These results highlight a need for a high-quality placebo-controlled trial to allow a definitive conclusion to be reached on the efficacy of risperidone and quetiapine for hyperactive delirium.
Emergency department															
Bervoets, C.	2015	Cross-sectional survey	Belgium	✓											There is no clear or systematic rationale for prescribing for acute agitation in Belgium. Practice in treating acute agitation shows a complex relationship with published evidence and guidelines. The level of agitation in patients and the type of physician prescribing the first pharmaceutical treatment both are clearly important variables and should be implemented in further research designs.
Campillo, A.	2012	Retrospective cohort study	United States									✓			There appeared to be limited effects on vital signs in this small sample when using a combination of haloperidol and lorazepam.
Chan, E.W.	2015	Cross-sectional survey	Hong Kong	✓											The use of haloperidol and benzodiazepines as monotherapy is common in the management of acute agitation in Hong Kong emergency departments. Prescribers' choice of sedation drugs are also more conservative and less variable overall. Future work could focus on clinical practice guideline development and training regarding the safe use of combination therapy.
Chan, E.W.	2011	Cross-sectional	Australia	✓											There is considerable variation in the management of hypothetical

		survey													cases of acute agitation in Australasian emergency departments. Benzodiazepines and antipsychotics, either alone or in combination, are commonly used. An Australasian clinical practice guideline was perceived as useful.
Cowling, M.	2019	Cross-sectional survey	United States	✓											Emergency department providers reported using haloperidol most often as a second line treatment to manage both acute and acute on chronic pain. When haloperidol was used as a first line agent, providers claimed that additional medicines were not usually required. Haloperidol may provide an effective alternative to opioids in treatment of acute pain and acute exacerbations of chronic pain in the emergency department.

*As reported in the study

Table 3.5 Reported Antipsychotic Medication Prescribing Indications for Included Studies, by Acute Care Setting

REPORTED ANTIPSYCHOTIC PRESCRIBING INDICATIONS	ACUTE CARE SETTING		
	Intensive care ¹ N=43	Inpatient ¹ N=21	Emergency department N=5
Delirium	34 (79%)	14 (67%)	0 (0%)
Agitation	9 (21%)	7 (33%)	4 (80%)
Sedation	5 (12%)	1 (5%)	0 (0%)
Sleep	5 (12%)	2 (10%)	0 (0%)
Palliation	0 (0%)	4 (19%)	0 (0%)
Alcohol withdrawal	1 (2%)	0 (0%)	0 (0%)
Pain	1 (2%)	1 (5%)	1 (20%)
Antiemetic	0 (0%)	2 (10%)	0 (0%)
Dementia	0 (0%)	1 (5%)	0 (0%)
Anxiety/panic	0 (0%)	1 (5%)	0 (0%)
Reduce falls	0 (0%)	1 (5%)	0 (0%)

Percentages do not add up to 100 due to the possibility of multiple outcomes per study

¹One primary study report outcomes for patients admitted as inpatients and in ICU

Table 3.6 Measured and Perceived Antipsychotics Prescribed and Prescribing Indications Reported for Included Studies, by Acute Care Setting

Intensive care																
First author	Year	Study type	Country/Continent	Prescribed antipsychotic medications		Antipsychotic indication										
				Perceived	Measured	Delirium	Agitation	Sedation	Sleep	Palliation	Alcohol withdrawal	Dementia	Antiemetic	Anxiety/Panic	Reduce falls	Pain
Almehairi, E.	2018	Cross-sectional survey + chart review	United Kingdom		Haloperidol Quetiapine Olanzapine	✓	✓									
Boncyk, C.S.	2021	Retrospective cohort study	United States		Haloperidol Quetiapine Olanzapine	✓										
Brown, G.	1998	Quasi-experimental study	Canada		Methotrimeprazine				✓							
Ceraso, D.H.	2010	Cross-sectional survey	South America [‡]	Haloperidol		✓										
Chawla, R.	2013	Cross-sectional survey	India	Haloperidol		✓										
Collet, M.O.	2019	Focus groups	Denmark	Haloperidol Olanzapine		✓	✓									
D'Angelo, R.G.	2019	Pre-post interventional study	United States		Haloperidol Quetiapine Olanzapine Risperidone	✓										
DeBacker, J.	2018	Retrospective cohort study	Canada		Haloperidol Quetiapine	✓										
Devlin, J.W.	2011	Cross-sectional survey	United States	Haloperidol Quetiapine Olanzapine		✓	✓									
Dyal, S.	2019	Cross-sectional survey	United States	Haloperidol							✓					
Dzierba, A.L.	2019	Cross-sectional survey	United States	Haloperidol		✓										
Eastwood, G.M.	2012	Quality improvement study	Australia		Haloperidol Quetiapine Olanzapine	✓										
Ely, E.W.	2004	Cross-sectional survey	United States	Haloperidol Quetiapine Olanzapine Risperidone		✓										
Farrokh, S.	2017	Retrospective cohort study	United States		Quetiapine Olanzapine Risperidone Aripiprazole Ziprasidone	Not reported										
Flores, D.J.	2015	Cross-sectional survey	United States	Haloperidol		✓										
Gilani, A.A.	2020	Cross-sectional	United Kingdom	Haloperidol Quetiapine		✓										

		survey		Olanzapine Risperidone Aripiprazole Ziprasidone												
Gilbert, B.	2017	Retrospective cohort study	United States		Haloperidol Quetiapine Olanzapine Risperidone	Not reported										
Gill, K.V.	2012	Cross-sectional survey + retrospective cohort study	United States	Haloperidol Quetiapine Olanzapine Risperidone	Haloperidol Quetiapine Olanzapine Risperidone			✓								
Glass, M.	2018	Pre-post interventional study	Not reported		Haloperidol	✓										
Gong, Z.	2009	Cross-sectional survey	China	Haloperidol Olanzapine		✓										
Johnson, K.	2016	Pre-post interventional study	United States	Haloperidol		✓										
Kim, D.H.	2018	Retrospective cohort study	United States		Haloperidol Quetiapine Olanzapine Risperidone Aripiprazole Ziprasidone	Not reported										
Kloet, M.A.	2017	Quality improvement study	United States		Risperidone	Not reported										
Kotfis, K.	2017	Cross-sectional survey	Poland	Haloperidol Quetiapine Olanzapine		✓										
Kram, B.L.	2015	Retrospective cohort study	United States		Quetiapine Olanzapine Risperidone Aripiprazole Ziprasidone	✓										
Kram, B.L.	2019	Quality improvement study	United States		Quetiapine Olanzapine Risperidone Aripiprazole	✓	✓	✓	✓							
Levine, A.R.	2019	Retrospective cohort study	United States		Quetiapine Olanzapine Risperidone	✓			✓							
Mac Sweeney, R.	2010	Cross-sectional survey	United Kingdom	Haloperidol		✓										
Marshall, J.	2016	Retrospective cohort study	United States		Haloperidol Quetiapine Olanzapine Risperidone Aripiprazole Ziprasidone	Not reported										
Mehta, S.	2007	Cross-sectional survey	Canada	Haloperidol					✓							
Mo, Y.	2017	Cross-sectional survey	United States	Haloperidol Quetiapine		✓	✓									

Palacios-Ceña, D.	2016	Focus groups	Spain	Haloperidol		✓										
Patel, M.	2019	Retrospective cohort study	Not reported		Quetiapine				✓							
Patel, R.P.	2009	Cross-sectional survey	United States	Haloperidol Quetiapine Olanzapine Risperidone Aripiprazole Ziprasidone		✓										
Ranzani, O.T.	2014	Quality improvement study	Brazil		Haloperidol			✓								
Rhoney, D.H.	2003	Cross-sectional survey	United States	Haloperidol			✓	✓								✓
Salluh, J.I.F.	2009	Cross-sectional survey	Brazil	Haloperidol		✓										
Selim, A.A.	2017	Cross-sectional survey	Egypt	Haloperidol		✓										
Silverman, D.	2013	Retrospective cohort study	United States		Quetiapine		✓									
Stuart, M.M.	2020	Quasi-experimental study (retrospective)	United States		Haloperidol Quetiapine Olanzapine Risperidone Ziprasidone	✓	✓									
Swan, J.T.	2012	Retrospective cohort study	United States		Haloperidol Quetiapine Olanzapine Risperidone Ziprasidone	✓										
Sztrymf, B.	2012	Cross-sectional survey	France	Haloperidol		✓										
Thiboutot, Z.	2016	Prospective cohort study	Canada		Haloperidol Quetiapine Olanzapine Risperidone		✓		✓							
Tomichek, J.E.	2016	Prospective cohort study	United States		Haloperidol Quetiapine Olanzapine Risperidone Ziprasidone	✓										
Trogrlic, Z.	2013	Cross-sectional survey	Netherlands	Haloperidol		✓										
Trogrlic, Z.	2013	Prospective cohort study	Netherlands		Haloperidol	✓										
van den Boogaard, M.	2009	Quality improvement study	Netherlands		Haloperidol	✓										
Wang, J.	2017	Cross-sectional survey	China	Haloperidol		✓										
Inpatient																
Al-Qadheeb, N.S.	2013	Prospective cohort study	United States		Haloperidol Quetiapine Olanzapine Risperidone	Not reported										

					Aripiprazole Ziprasidone											
Basciotta, M.	2018	Retrospective cohort study	United States		Haloperidol Quetiapine Olanzapine Risperidone Aripiprazole Ziprasidone	Not reported										
Bascom, P.B.	2014	Case report or case series	USA	Haloperidol Quetiapine Olanzapine Risperidone		✓	✓			✓						
Bedouch, P.	2015	Cross-sectional survey	France	Haloperidol		Not reported										
Birigen, E.K.	2021	Cross-sectional survey	United States	Haloperidol Quetiapine Olanzapine					✓				✓	✓		✓
Brennan, M.	2018	Case-control	USA		Haloperidol Quetiapine Olanzapine Risperidone	✓									✓	
Brett, J.	2020	Retrospective cohort study + chart review	Australia		Quetiapine	✓	✓									
Briskman, I.	2010	Retrospective cohort study	Israel		Haloperidol Risperidone	✓										
Costa-Dias, M.J.	2014	Retrospective cohort study	Portugal		Haloperidol	Not reported										
Fontaine, G.V.	2018	Retrospective cohort study	United States		Haloperidol Quetiapine Olanzapine Risperidone Ziprasidone	Not reported										
Herzig, S.J.	2016	Retrospective cohort study	United States		Haloperidol Quetiapine Olanzapine Risperidone Aripiprazole Ziprasidone	✓					✓					
Hosie, A.	2021	Cross-sectional survey	Australia (All)	Haloperidol Quetiapine Olanzapine Risperidone		✓				✓						
Hui, D.	2011	Retrospective cohort study	United States		Haloperidol Olanzapine	✓		✓								
Kuscu, M.K.	2004	Cross sectional survey + semi-structured interviews	Turkey	Haloperidol Olanzapine Risperidone		✓										
Loh, E.C.	2011	Case report or case series	Malaysia	Olanzapine			✓			✓						
Loh, K.P.	2016	Retrospective cohort study + chart review	United States		Haloperidol Quetiapine Olanzapine Risperidone	✓										
Masman, A.D.	2015	Retrospective cohort study	Netherlands		Haloperidol					✓						
Mattison, M.L.P.	2014	Pre-post	United States		Haloperidol		✓									

		control interventional study														
McNeill, R.	2021	Retrospective cohort study	New Zealand		Haloperidol								✓			
Meagher, D.	2013	Cross- sectional survey	Europe†	Haloperidol Risperidone		✓										
Someya, T.	2001	Cross- sectional cohort study	Japan	Haloperidol		✓	✓									
Thacker, S.	1996	Cross- sectional survey	United Kingdom	Haloperidol			✓									
Trenaman, S.C.	2018	Cross- sectional cohort study	Canada		Haloperidol Quetiapine Olanzapine Risperidone Methotrimeprazine	Not reported										
Tropea, J.	2009	Medical record audit	Australia		Haloperidol Quetiapine Olanzapine Risperidone	✓										
Weir, D.L.	2020	Prospective cohort study	Canada		Quetiapine Olanzapine Risperidone Aripiprazole	✓										
Wong, A.	2014	Retrospective cohort study	Canada		Olanzapine		✓									
Yasuyuki, O.	2016	Cross- sectional survey	Japan	Haloperidol Olanzapine Risperidone Aripiprazole Methotrimeprazine		✓										
Emergency department																
Bervoets, C.	2015	Cross- sectional survey	Belgium	Haloperidol Quetiapine Olanzapine Risperidone Aripiprazole			✓									
Campillo, A.	2012	Retrospective cohort study	United States		Haloperidol		✓									
Chan, E.W.	2015	Cross- sectional survey	Hong Kong	Haloperidol			✓									
Chan, E.W.	2011	Cross- sectional survey	Australia	Haloperidol			✓									
Cowling, M.	2019	Cross- sectional survey	United States	Haloperidol												✓

Table 3.7 Number of Studies Reporting on Healthcare Professional Reported Perceived Antipsychotic Prescribing Practices, by Acute Care Setting and Antipsychotic Type

PERCEIVED ANTIPSYCHOTIC PRESCRIBING PRACTICES							
N= 36							
ACUTE CARE SETTING	Haloperidol N= 36	Quetiapine N= 11	Olanzapine N= 12	Risperidone N= 10	Ziprasidone N= 2	Aripiprazole N= 4	Methotrimeprazine N= 1
Intensive care N= 24	24 (100%)	7 (29%)	8 (33%)	4 (17%)	2 (10%)	2 (8%)	0 (0%)
Inpatient N= 8	8 (100%)	3 (38%)	3 (38%)	5 (63%)	0 (0%)	1 (13%)	1 (13%)
Emergency department N= 4	4 (100%)	1 (25%)	1 (25%)	1 (25%)	0 (0%)	1 (25%)	0 (0%)

Percentages do not add up to 100 due to the possibility of multiple outcomes per study

Table 3.8 Number of Studies Reporting on Measured Outcomes of Antipsychotic Prescribing Practices, by Acute Care Setting and Antipsychotic Type

MEASURED ANTIPSYCHOTIC PRESCRIBING PRACTICES							
N= 34							
ACUTE CARE SETTING	Haloperidol N= 26	Quetiapine N= 26	Olanzapine N= 23	Risperidone N= 22	Ziprasidone N= 11	Aripiprazole N= 8	Methotrimeprazine N= 0
Intensive care N= 20	14 (70%)	17 (85%)	14 (70%)	13 (65%)	7 (35%)	5 (25%)	0 (0%)
Inpatient N= 14	12 (86%)	9 (64%)	9 (64%)	9 (64%)	4 (29%)	3 (21%)	0 (0%)
Emergency department N= 0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Percentages do not add up to 100 due to the possibility

Table 3.9 Reported Additionally Prescribed Sedative Hypnotic Medications for Included Studies Reporting on Antipsychotic Medication Prescribing, by Acute Care Setting

REPORTED ADDITIONAL SEDATIVE HYPNOTIC MEDICATIONS	ACUTE CARE SETTING		
	Intensive care N=28	Inpatient N=15	Emergency department N=1
Benzodiazepines	24 (86%)	8 (53%)	1 (0%)
Intravenous sedative infusions ¹	9 (32%)	0 (0%)	0 (0%)
Opioid pain medications	8 (29%)	2 (13%)	0 (0%)
Dexmedetomidine	8 (29%)	1 (7%)	0 (0%)
Another antipsychotic	7 (25%)	8 (53%)	0 (0%)
Sleep aids	2 (7%)	1 (7%)	0 (0%)
Other sedatives ²	2 (7%)	3 (20%)	0 (0%)
Clonidine	1 (4%)	1 (7%)	0 (0%)

Percentages do not add up to 100 due to the possibility of multiple outcomes per study

¹Reported propofol and ketamine infusions

²Reported barbiturates and hydroxyzine

Table 3.10 Reported Co-Prescribed Sedative Hypnotic Medications with Antipsychotic Medications for Included Studies Which Report on Additionally Prescribed Medications, by Acute Care Setting

First author	Year	Study type	Country/Continent	Intensive Care							
				Reported additional sedative hypnotic medications							
				Benzodiazepines	Intravenous sedative infusions ¹	Opioid pain medications	Dexmedetomidine	Another antipsychotic	Sleep aids	Other sedatives ²	Clonidine
Boncyk, C.S.	2021	Retrospective cohort study	United States					✓			
Brown, G.	1998	Quasi-experimental study	Canada	✓				✓			
Ceraso, D.H.	2010	Cross-sectional survey	South America [†]	✓			✓	✓			
Collet, M.O.	2019	Focus groups	Denmark	✓							
D'Angelo, R.G.	2019	Pre-post interventional study	United States	✓		✓					
DeBacker, J.	2018	Retrospective cohort study	Canada	✓	✓	✓					
Devlin, J.W.	2011	Cross-sectional survey	United States	✓			✓	✓			
Dyal, S.	2019	Cross-sectional survey	United States	✓				✓		✓	✓
Dzierba, A.L.	2019	Cross-sectional survey	United States	✓	✓		✓				
Ely, E.W.	2004	Cross-sectional survey	United States	✓							
Farrokh, S.	2017	Retrospective cohort study	United States					✓			
Gilani, A.A.	2020	Cross-sectional survey	United Kingdom					✓			
Gilbert, B.	2017	Retrospective cohort study	United States	✓					✓		
Gill, K.V.	2012	Cross-sectional survey + retrospective cohort study	United States	✓	✓						
Glass, M.	2018	Pre-post interventional study	Not reported	✓							
Levine, A.R.	2019	Retrospective cohort study	United States	✓		✓					
Mac Sweeney, R.	2010	Cross-sectional survey	United Kingdom	✓	✓						

Mehta, S.	2007	Cross-sectional survey	Canada	✓		✓					
Mo, Y.	2017	Cross-sectional survey	United States	✓	✓		✓				
Patel, M.	2019	Retrospective cohort study	Not reported						✓		
Patel, R.P.	2009	Cross-sectional survey	United States	✓	✓	✓	✓				
Ranzani, O.T.	2014	Quality improvement study	Brazil	✓	✓		✓				
Rhoney, D.H.	2003	Cross-sectional survey	United States	✓	✓	✓					
Salluh, J.I.F.	2009	Cross-sectional survey	Brazil	✓	✓		✓				
Silverman, D.	2013	Retrospective cohort study	United States	✓							
Sztrymf, B.	2012	Cross-sectional survey	France	✓						✓	
Troglic, Z.	2013	Prospective cohort study	Netherlands	✓							
Wang, J.	2017	Cross-sectional survey	China	✓			✓				
Inpatient											
Al-Qadheeb, N.S.	2013	Prospective cohort study	United States	✓							
Bascom, P.B.	2014	Case report or case series	USA	✓		✓				✓	
Brennan, M.	2018	Case-control	USA					✓			
Fontaine, G.V.	2018	Retrospective cohort study	United States					✓			
Hosie, A.	2021	Cross-sectional survey	Australia (All)	✓			✓		✓	✓	✓
Hui, D.	2011	Retrospective cohort study	United States	✓						✓	
Kuscu, M.K.	2004	Cross sectional survey + semi-structured interviews	Turkey	✓							
Loh, E.C.	2011	Case report or case series	Malaysia					✓			
Masman, A.D.	2015	Retrospective cohort study	Netherlands	✓		✓		✓			
Meagher, D.	2013	Cross-sectional survey	Europe [†]					✓			
Thacker, S.	1996	Cross-sectional survey	United Kingdom	✓				✓			

Trenaman, S.C.	2018	Cross-sectional cohort study	Canada					✓			
Tropea, J.	2009	Medical record audit	Australia	✓				✓			
Emergency department											
Chan, E.W.	2011	Cross-sectional survey	Australia	✓							

¹Reported propofol and ketamine infusions

²Reported barbiturates and hydroxyzine

Table 3.11 Domains and Constructs According to the Theoretical Domains Framework of Perceptions on Antipsychotic Prescribing from Healthcare Professionals for Included studies, by Acute Care Setting

	Intensive care	Inpatient	Emergency department
Perspectives ¹	N=18	N=7	N=4
Knowledge	14 (77%)	6 (86%)	3 (75%)
Knowledge of condition/scientific rationale	14 (100%)	6 (100%)	3 (100%)
Skills	8 (44%)	2 (29%)	2 (50%)
Skill development	3 (38%)	0 (0%)	0 (0%)
Competence	4 (50%)	1 (50%)	1 (50%)
Ability	1 (13%)	0 (0%)	0 (0%)
Skill assessment	0 (0%)	0 (0%)	1 (50%)
Interpersonal skills	0 (0%)	1 (50%)	0 (0%)
Social/Professional Role and Identity	9 (53%)	4 (50%)	3 (75%)
Professional role	4 (44%)	2 (50%)	1 (33%)
Professional confidence	4 (44%)	1 (25%)	2 (67%)
Leadership	1 (11%)	1 (25%)	0 (0%)
Beliefs about Capabilities	16 (89%)	5 (71%)	4 (100%)
Perceived competence	13 (81%)	3 (60%)	4 (100%)
Self-efficacy	2 (13%)	0 (0%)	0 (0%)
Perceived behavioural control	1 (6%)	1 (20%)	0 (0%)
Beliefs	1 (6%)	1 (20%)	0 (0%)
Empowerment	1 (6%)	0 (0%)	0 (0%)
Optimism	0 (0%)	1 (13%)	0 (0%)
Beliefs about Consequences	14 (78%)	6 (86%)	3 (75%)
Beliefs	6 (43%)	3 (50%)	0 (0%)
Consequences	7 (50%)	4 (67%)	2 (67%)
Outcome expectancies	2 (11%)	0 (0%)	1 (33%)
Reinforcement	5 (29%)	1 (13%)	2 (50%)
Rewards	2 (40%)	1 (100%)	1 (50%)
Reinforcement	3 (60%)	0 (0%)	1 (50%)
Intentions	1 (6%)	1 (13%)	0 (0%)
Stability of intentions	0 (0%)	0 (0%)	0 (0%)
Stages of change model	1 (100%)	1 (100%)	0 (0%)
Goals	2 (12%)	3 (38%)	1 (25%)
Goal priority	2 (100%)	2 (67%)	0 (0%)
Goal/target setting	0 (0%)	1 (33%)	1 (100%)
Memory, Attention & Decision Processes	7 (41%)	2 (25%)	1 (25%)
Decision making	5 (71%)	2 (100%)	1 (100%)
Cognitive overload/tiredness	1 (14%)	0 (0%)	0 (0%)
Attention	1 (14%)	0 (0%)	0 (0%)
Environmental Context & Resources	16 (94%)	2 (25%)	3 (75%)
Environmental stressors	1 (6%)	0 (0%)	0 (0%)
Resources/material resources	12 (75%)	1 (50%)	3 (100%)
Organizational culture/climate	1 (6%)	0 (0%)	0 (0%)
Person-environment Interaction	1 (6%)	0 (0%)	0 (0%)
Facilitators and barriers	1 (6%)	1 (50%)	0 (0%)
Social Influences	8 (47%)	2 (25%)	3 (75%)
Group norms	3 (38%)	1 (50%)	2 (67%)
Group conformity	2 (25%)	0 (0%)	1 (33%)
Social comparisons	1 (13%)	1 (50%)	0 (0%)
Alienation	2 (25%)	0 (0%)	0 (0%)
Intergroup conflict	1 (13%)	0 (0%)	0 (0%)
Emotion	3 (18%)	2 (25%)	0 (0%)
Stress	2 (67%)	1 (50%)	0 (0%)

Fear	1 (33%)	1 (50%)	0 (0%)
Behavioural Regulation	4 (24%)	3 (38%)	1 (25%)
Self-monitoring	3 (75%)	2 (67%)	1 (100%)
Action planning	1 (25%)	1 (33%)	0 (0%)

Percentages do not add up to 100 due to the possibility of multiple outcomes per study

¹Perspectives determined from deductive thematic analysis using the Theoretical Domains Framework of included studies

Table 3.12 Deductive Thematic Analysis Using the Theoretical Domains Framework on Perceptions on Antipsychotic Prescribing for Included Studies

Domains and constructs ¹																
First author	Year	Clinical specialty	Knowledge	Skills	Social/Professional Role	Beliefs about Capabilities	Optimism	Beliefs about Consequences	Reinforcement	Intentions	Goals	Memory, Attention & Decision Processes	Environmental Context & Resources	Social Influences	Emotion	Behavioural Regulation
Intensive care																
Almehairi, E.	2018	Intensive care	x	x	x	✓ (Perceived behavioural control)	x	x	x	x	x	x	✓ (Resources/material resources)	x	x	x
Ceraso, D.H.	2010	Intensive care	✓ (Knowledge)	x	✓ (Professional role)	✓ (Perceived competence)	x	✓ (Consequences)	x	x	x	x	✓ (Resources/material resources)	x	x	x
Chawla, R.	2013	Intensive care	x	x	x	✓ (Perceived competence)	x	✓ (Beliefs)	x	x	x	x	✓ (Resources/material resources)	x	x	x
Collet, M.O.	2019	Intensive care	x	✓ (Ability)	✓ (Professional confidence)	✓ (Perceived competence)	x	✓ (Consequences)	✓ (Rewards)	x	✓ (Goal priority)	✓ (Decision making)	✓ (Resources/material resources)	✓ (Social comparisons)	✓ (Fear)	✓ (Self-monitoring)
Devlin, J.W.	2011	Intensive care	✓ (Knowledge)	✓ (Competence)	✓ (Professional role)	✓ (Perceived competence)	x	✓ (Beliefs)	✓ (Rewards)	x	x	✓ (Decision making)	✓ (Resources/material resources)	x	x	✓ (Action planning)
Ely, E.W.	2004	Intensive care	✓ (Knowledge)	x	✓ (Professional role)	✓ (Perceived competence)	x	✓ (Beliefs; consequences)	✓ (Reinforcement)	x	x	x	✓ (Resources/material resources)	x	x	x
Flores, D.J.	2015	Intensive care	✓ (Knowledge)	✓ (Skill development)	x	✓ (Perceived competence)	x	✓ (Outcome expectancies)	x	x	x	x	✓ (Barriers and facilitators)	✓ (Alienation)	x	x
Gilani, A.A.	2020	Intensive care	x	x	x	x	x	x	x	x	x	✓ (Cognitive overload/tiredness)	✓ (Resources/material resources)	x	✓ (Stress)	✓ (Self-monitoring)
Gill, K.V.	2012	Intensive care	✓ (Knowledge)	x	x	x	x	x	✓ (Reinforcement)	✓ (Stages of change model)	x	✓ (Decision making)	✓ (Organizational culture/climate)	✓ (Group norms)	x	x
Johnson, K.	2016	Intensive care	✓ (Knowledge)	✓ (Skill development)	x	✓ (Perceived competence)	x	✓ (Consequences)	x	x	x	x	x	x	x	x
Mehta, S.	2007	Intensive care	✓ (Knowledge)	✓ (Competence)	✓ (Professional confidence)	✓ (Self-efficacy)	x	✓ (Beliefs)	x	x	x	✓ (Decision making)	✓ (Resources/material resources)	✓ (Group conformity)	x	x
Mo, Y.	2017	Intensive care	✓ (Knowledge)	✓ (Skill assessment)	x	✓ (Perceived competence)	x	✓ (Beliefs)	x	x	✓ (Goal priority)	✓ (Decision making)	✓ (Resources/material resources)	x	x	x
Palacios-Ceña, D.	2016	Intensive care	✓ (Knowledge)	✓ (Competence)	✓ (Professional role)	✓ (Perceived competence)	x	✓ (Beliefs)	x	x	x	✓ (Attention)	✓ (Person-environment interaction)	✓ (Group conformity; alienation)	✓ (Stress)	✓ (Self-monitoring)
Patel, R.P.	2009	Intensive care	✓ (Knowledge)	x	x	✓ (Perceived competence)	x	✓ (Consequences)	x	x	x	x	✓ (Resources/material resources)	x	x	x
Ranzani, O.T.	2014	Intensive care	✓ (Knowledge)	✓ (Competence)	✓ (Leadership)	✓ (Self-efficacy; perceived competence)	x	x	x	x	x	x	✓ (Resources/material resources)	✓ (Intergroup conflict)	x	x
Sztrymf, B.	2012	Intensive care	✓ (Knowledge)	x	✓ (Professional confidence)	✓ (Perceived competence)	x	✓ (Consequences)	✓ (Reinforcement)	x	x	x	✓ (Environmental stressors)	✓ (Group norms)	x	x
Trogrlic, Z.	2013	Intensive care	✓ (Knowledge)	x	x	✓ (Empowerment;	x	✓ (Outcome expectancies)	x	x	x	x	x	x	x	x

						perceived competence										
Wang, J.	2017	Intensive care	✓ (Knowledge)	x	✓ (Professional confidence)	✓ (Beliefs)	x	✓ (Consequences)	x	x	x	x	✓ (Resources/material resources)	✓ (Group norms)	x	x
Inpatient																
Bascom, P.B.	2014	Inpatient	✓ (Knowledge)	✓ (Competence)	✓ (Professional role)	x	x	✓ (Consequences)	x	x	✓ (Goal priority)	x	x	x	✓ (Fear)	x
Birigen, E.K.	2021	Inpatient	✓ (Knowledge)	x	✓ (Professional confidence)	✓ (Perceived competence)	x	✓ (Consequences)	x	x	x	✓ (Decision making)	✓ (Resources/material resources)	✓ (Group norms)	x	✓ (Action planning)
Hosie, A.	2021	Inpatient	✓ (Knowledge)	✓ (Interpersonal skills)	✓ (Leadership)	✓ (Perceived competence)	✓ (Optimism)	✓ (Consequences)	x	✓ (Stages of change model)	✓ (Goal/target setting)	✓ (Decision making)	✓ (Resources/material resources)	✓ (Social comparisons)	✓ (Stress)	x
Loh, E.C.	2011	Inpatient	x	x	✓ (Professional role)	x	x	✓ (Beliefs)	x	x	✓ (Goal priority)	x	x	x	x	x
Meagher, D.	2013	Inpatient	✓ (Knowledge)	x	x	✓ (Perceived competence)	x	x	x	x	x	x	x	x	x	x
Someya, T.	2001	Inpatient	✓ (Knowledge)	x	x	✓ (Beliefs)	x	✓ (Beliefs)	✓ (Rewards)	x	x	x	x	x	x	✓ (Action planning)
Yasuyuki, O.	2016	Inpatient	✓ (Knowledge)	x	x	✓ (Perceived behavioural control)	x	✓ (Beliefs)	x	x	x	x	x	x	x	✓ (Self-monitoring)
Emergency department																
Bervoets, C.	2015	Emergency department	✓ (Knowledge)	x	✓ (Professional role)	✓ (Perceived competence)	x	✓ (Consequences)	x	x	x	x	x	✓ (Group norms)	x	✓ (Self-monitoring)
Chan, E.W.	2015	Emergency department	x	x	x	✓ (Perceived competence)	x	x	x	x	x	x	✓ (Resources/material resources)	✓ (Group conformity)	x	x
Chan, E.W.	2011	Emergency department	✓ (Knowledge)	✓ (Competence)	✓ (Professional confidence)	✓ (Perceived competence)	x	✓ (Consequences)	✓ (Reinforcement)	x	x	x	✓ (Resources/material resources)	✓ (Group norms)	x	x
Cowling, M.	2019	Emergency department	✓ (Knowledge)	✓ (Skill assessment)	x	✓ (Perceived competence)	x	x	✓ (Rewards)	x	✓ (Goal/target setting)	✓ (Decision making)	x	x	x	x

¹Constructs reported in parentheses of appropriate domains

Table 3.13 Description of Reported Antipsychotic Deprescribing Strategies Applied in Parallel for Included Studies Reporting on Antipsychotic Medication Prescribing

First author	Year	Study Location	Clinical speciality	Deprescribing strategies
D'Angelo, R.G.	2019	United States	Intensive care	1. Antipsychotic discontinuation algorithm implemented before ICU transfer 2. Multidisciplinary education of algorithm
Kram, B.L.	2019	United States	Intensive care	1. Pharmacy-based electronic handoff tool 2. Pharmacist education on ICU delirium and consensus guidelines for antipsychotic use
Stuart, M.M.	2020	United States	Intensive care	1. Pharmacist-driven prescriptive authority to discontinue or taper antipsychotic medication following resolution of delirium 2. Collaborative practice agreement between physicians and pharmacists

Figure 3.1 Study Selection Flow Chart

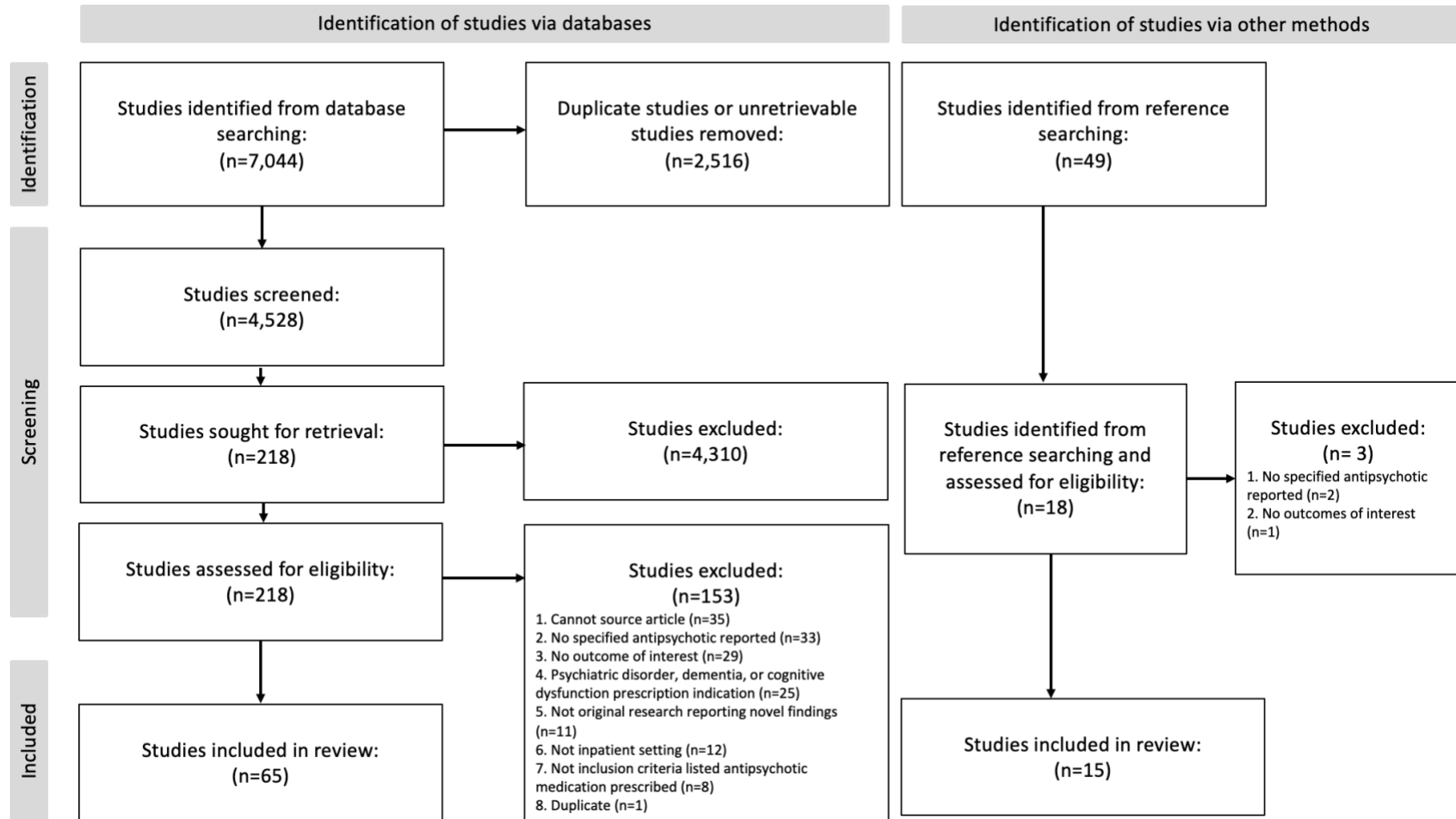


Figure 3.2 Studies Reporting on Antipsychotic Medication Prescribing Practices Over Time, by Antipsychotic Type

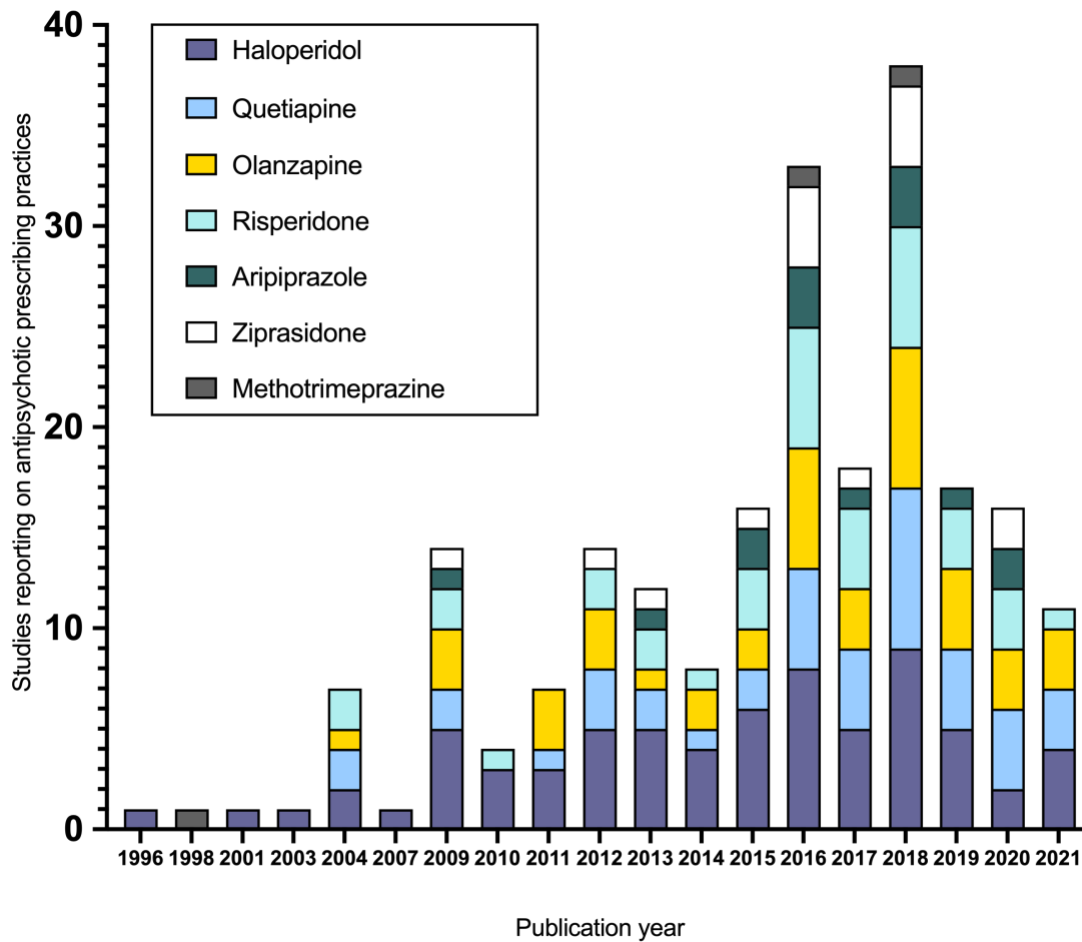


Figure 3.3 Continents and Acute Care Settings Represented Among Included Studies

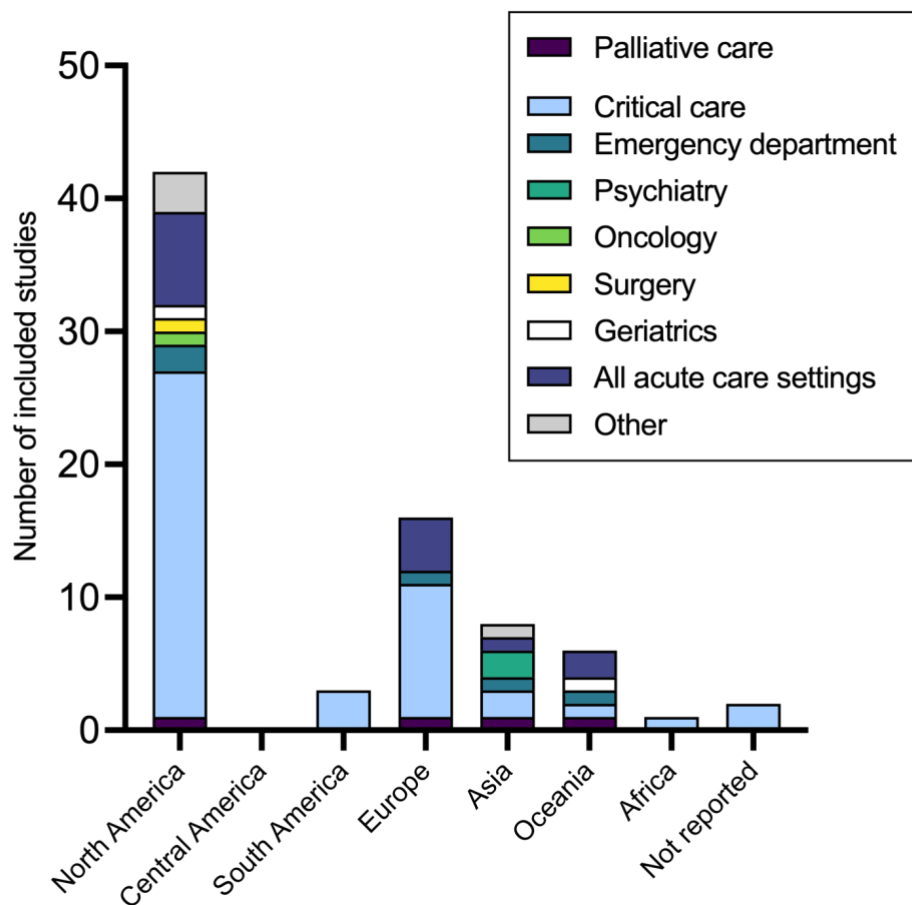
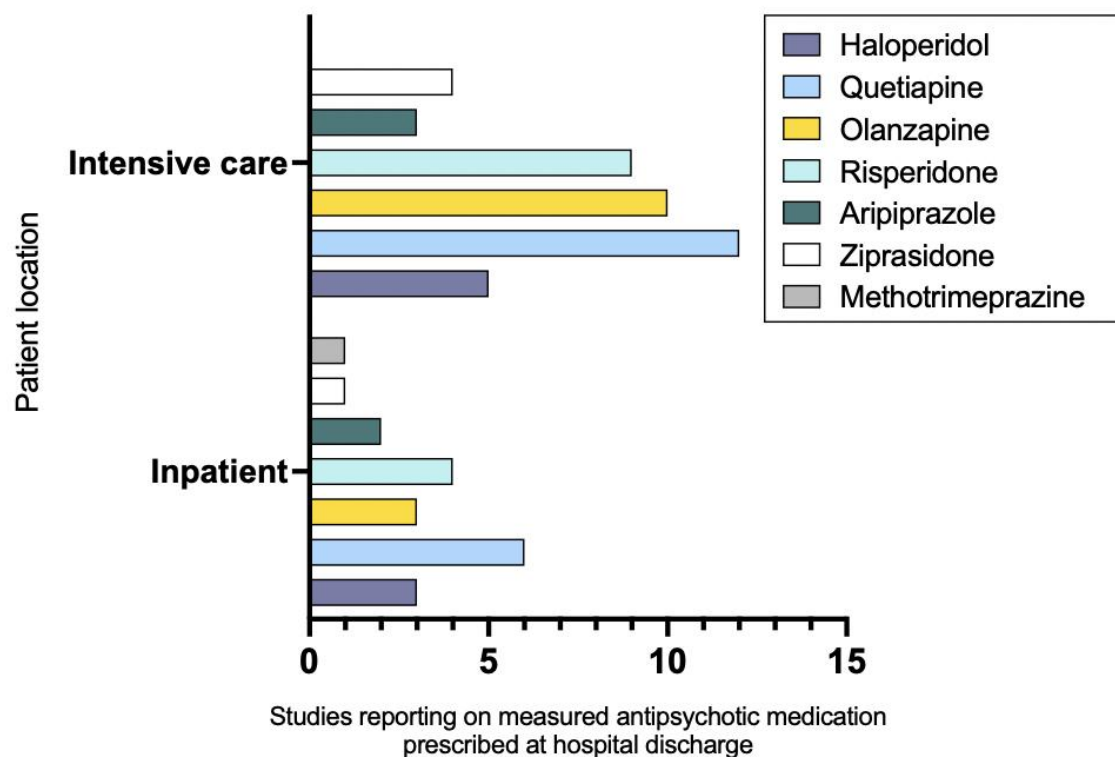
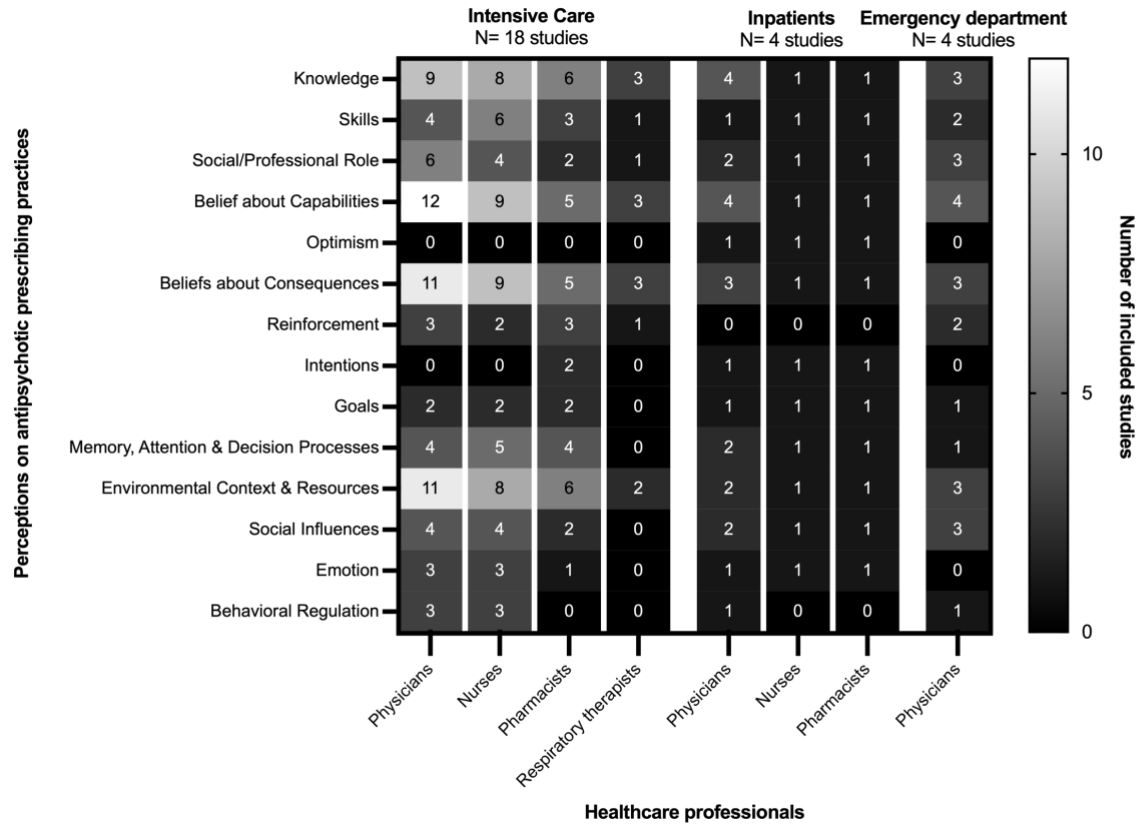


Figure 3.4 Measured Antipsychotic Medications Prescribed at Hospital Discharge for Included Studies on Antipsychotic Prescribing Practices, by Acute Care Setting¹



¹Patient location defined as the primary location patients were first admitted and started on antipsychotic medications. Patients admitted to intensive care were either discharged directly home or to the hospital ward before hospital discharge. Patients admitted to inpatient setting were never admitted to intensive care. No studies reporting measured outcomes included patients from the emergency department setting.

Figure 3.5 Total Number of Studies¹ Reporting on Perceptions Toward Antipsychotic Prescribing Practices According to the Theoretical Domains Framework, by Acute Care Setting and Healthcare Professional Role



¹Four unique studies not included due to no reporting of healthcare professional role

Appendix 3.1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	1-2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	3-4
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	4
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	4
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	5-6
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	6
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Table 3.1
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	7-8
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any	7-8

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
		processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	8
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	Not applicable
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	8-9
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	9, Figure 1
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	10-11
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	Not applicable
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	Tables 3.1-3.13
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	10-13
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	13-15
Limitations	20	Discuss the limitations of the scoping review process.	15-16
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	16
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	17

JB1 = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

Appendix 3.2 Pre-specified Antipsychotic Medications Evaluated in Search Strategy

Selected antipsychotic medications for evaluation
Haloperidol/Haldol®
Quetiapine/Seroquel® (immediate release and extended release)
Risperidone/Risperidal® (immediate release and extended release)
Ziprasidone/Zeldox®/Geodon®
Aripiprazole/Abilify®
Olanzapine/Zyprexa®
Methotrimeprazine/Nozinan®

Appendix 3.3 Alphabetical References for Included Studies

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CHAPTER 4: A NATIONWIDE MODIFIED DELPHI CONSENSUS PROCESS TO PRIORITIZE EXPERIENCES AND INTERVENTIONS FOR ANTIPSYCHOTIC MEDICATION DEPRESCRIBING AMONG CRITICALLY ILL ADULT PATIENTS

Jaworska N., Makuk K., Krewulak KD., Niven DJ., Ismail Z., Burry LD., Mehta S., Fiest KM. A nationwide modified Delphi consensus process to prioritize experiences and interventions for antipsychotic medication deprescribing among critically ill adult patients. *Prepared for submission.*

4.1 Abstract

Background: Antipsychotic medications are frequently prescribed to critically ill patients which subsequently leads to their continuation at transitions of care thereafter. The aim of this study was to generate evidence-informed consensus statements with key stakeholders on antipsychotic minimization and deprescribing for ICU patients.

Methods: Three rounds of online surveys were completed in a modified Delphi consensus process with 57 key stakeholders (physicians, nurses, and pharmacists) who work with ICU patients. During Rounds 1 and 2, participants used a 9-point Likert scale (1–strongly disagree, 9–strongly agree) to rate perceptions related to antipsychotic prescribing (i.e., experiences related to delivery of patient care), knowledge and frequency of antipsychotic use, knowledge surrounding antipsychotic guideline recommendations, and strategies (i.e., interventions addressing current antipsychotic prescribing practices) for antipsychotic minimization and deprescribing. Participants used free-text boxes to refine and suggest additional perceptions and/or strategies. Consensus was defined as a median score of 1–3 or 7–9. During Round 3, participants ranked statements on antipsychotic minimization and deprescribing strategies that achieved consensus with a median score 7–9 in previous rounds using a weighted ranking scale (0–100 points) to determine priority interventions. Statements pertaining to perceptions on antipsychotic medication use were not ranked in Round 3.

Results: Participants perceived patient and staff safety, patient sleep, and clinician concern for team members caring for agitated patients as common indications for antipsychotic use. Participants prioritized six strategies for consideration when developing and implementing interventions to guide antipsychotic minimization and deprescribing. Strategies focused on limiting antipsychotic prescribing to patients (1) with hyperactive delirium, (2) at risk to themselves, their family, and/or staff due to agitation, and (3) whose care and treatment are being impacted due to agitation or delirium, and prioritizing (4) communication among staff

about antipsychotic effectiveness, (5) direct and efficient communication tools on antipsychotic deprescribing at transitions of care, and (6) medication reconciliation at transitions of care.

Conclusions: We engaged diverse key stakeholders to generate evidence-informed consensus statements regarding antipsychotic prescribing perceptions and practices that can be utilized to implement interventions to promote antipsychotic minimization and deprescribing strategies for ICU patients with and following critical illness.

4.2 Background

Antipsychotic medications are frequently prescribed for critically ill patients to manage symptoms related to delirium and agitation [1-5], though it is well-established that antipsychotic medications do not alter delirium outcomes [6-11]. Current guidelines recommend against routine antipsychotic use in this patient population [12]. Antipsychotics are also increasingly being prescribed as sleep aids in critically ill patients [13], despite limited data to support this indication. Approximately one in three patients newly prescribed an antipsychotic medication in the ICU will be discharged from hospital with an ongoing prescription where the clinical indication for ongoing use is not clear [1, 14, 15]. Long-term antipsychotic medication use in non-critically ill older patients increases the risk of stroke, cardiovascular events, and sudden cardiac death [16-18]. Evidence-informed guidance on strategies to promote antipsychotic minimization and deprescribing to limit potentially inappropriate long-term antipsychotic therapy in critically ill patients after critical illness is currently lacking.

The ICU environment presents a unique challenge with respect to medication management. Critically ill patients are exposed to twice as many medications as non-critically ill patients and may be unable to actively participate in their medical care due to delirium, sedation

exposure, and/or the severity of illness [19, 20]. Time-limited use of antipsychotics may be necessary in critically ill patients with severe agitation due to anxiety or hallucinations who are at risk of harm to themselves or staff [12]. Additionally, transitions of care— where patients move from a resource rich environment to an environment with fewer available resources – are high risk periods for medication errors and continuation of potentially inappropriate medications such as antipsychotics [21, 22]. Insufficient communication of information at transitions of care can lead to medication errors during and following hospitalization and can contribute to polypharmacy, adverse drug events, and hospital readmission [23-25].

Restricting prescribing of antipsychotic medications in the setting of a clinically challenging environment where there may be few pharmacologic alternatives for the management of hyperactive delirium and agitation is unlikely to promote judicious antipsychotic prescribing practices nor limit continuation of potentially inappropriate antipsychotic medications [26]. By engaging healthcare professionals in the process of defining appropriate antipsychotic prescribing and deprescribing practices, key clinically relevant facilitators and barriers to antipsychotic minimization and deprescribing may be identified and targeted. We embarked on a program of research to understand the factors influencing healthcare professionals' antipsychotic prescribing and deprescribing practices and to review the relevant literature exploring healthcare professional perceptions and practices related to antipsychotic prescribing and deprescribing [27, 28]. With input from key stakeholders including physicians, nurses, and pharmacists, we aimed to develop evidence-informed, consensus-based statements on strategies to promote antipsychotic minimization and facilitate deprescribing for patients with and following critical illness.

4.3 Methods

4.3.1 Selection of Key Stakeholders

Stakeholders who engage in prescribing and/or deprescribing of antipsychotic medications and delirium management for adult patients with (i.e., ICU) and/or following (i.e., ward) critical illness in Canada were invited to participate. Participants were eligible to participate if they were aged 18 years or greater, English-speaking, a physician, nurse, or pharmacist who cared for adult critically ill patients with and/or following critical illness and were able to provide informed consent. We purposively recruited participants by contacting professional societies (Canadian Critical Care Society, Canadian Association of Critical Care Nurses) and through non-traditional means including social media (i.e., Twitter, Facebook). Participants from prior semi-structured individual interviews on antipsychotic prescribing practices completed by the research team [27] were also invited to participate via email.

4.3.2 Study Design

We conducted a virtual modified Delphi consensus process aligned with the RAND-UCLA appropriateness methodology [29] and reported our results in accordance with the Conducting and REporting DElphi Studies guidelines [30] (**Appendix 4.1**). Initial statements were generated following thematic analysis of a scoping review and semi-structured individual interviews [27, 28] conducted by the research team. The overall modified Delphi consensus process is shown in **Figure 4.1**. The statements consisted of seven themes divided into three domains: 1) Perceptions on antipsychotic medication use (n= 23 statements), 2) triggers for antipsychotic prescription (n= 19), and 3) antipsychotic minimization and deprescribing activities (n= 20). Participants reviewed and rated (based on perceived importance of individual statements) perceptions on antipsychotic medication prescribing, triggers for antipsychotic

prescribing, and antipsychotic minimization and deprescribing strategies during two of three rounds of voting. Participants subsequently ranked (based on perceived order of importance) triggers for antipsychotic prescribing and antipsychotic minimization and deprescribing strategies during the third round of voting in the modified Delphi consensus process. Statements were rated based on importance of individual statements on a 9-point Likert scale where 1 signified strongly disagree and 9 signified strongly agree. Ranking of statements was completed using a 100-point scale where participants ordered statements by importance relative to other consensus statements in the same theme. Participants were offered the opportunity to provide textual comments and additional statements during the first round, which were then incorporated into pre-existing statements or generated as new statements for subsequent rating. Three rounds of voting were completed between February and April 2022 with all rounds taking place via emailed self-administered surveys using a secure and encrypted online survey platform (Qualtrics, Provo, UT). Details for each round are included in **Appendices 4.2-4.4**. All surveys were developed and pilot-tested by research team members including physicians, nurses, and pharmacists to ensure that statements were clear and comprehensive. Participants provided informed consent prior to participating in each round of the modified Delphi consensus process. This study was approved by the University of Calgary Conjoint Health Research Ethics Board (REB21-0963).

4.3.3 Data Analysis

After each round of voting, participants were emailed a summary of aggregate results containing median rating or mean ranking scores for each statement. During Rounds 1 and 2 where statements were rated based on importance, we defined consensus *a priori* as any statement with a median score of 1–3 signifying non-significance or 7–9 signifying high significance. Statements achieving a median score of 4–6 in Round 1 were re-rated in Round 2.

Statements with a median score between whole number integers were rounded up to the next whole number if ≥ 0.5 and rounded down to the previous whole number if < 0.5 . During Round 3, individual statements achieving consensus with a median score of 7–9 in prior rounds were ranked. Consensus statements were ranked based on order of importance where we defined a statement to have priority if the statement's mean ranking was equal to or greater than one standard deviation above the theme's mean ranking to ensure that themes with unequal numbers of statements were equalized [31, 32]. Data analysis was conducted using Microsoft Excel (Microsoft Corporation, Redmond, WA).

4.4 Results

4.4.1 Participant Characteristics

Fifty-seven (100%) participants completed Round 1, 48 (82.5%) participants completed Round 2, and 30 (52.6%) participants completed Round 3 of the modified Delphi consensus process. Participants from eight provinces and all stakeholder groups were represented (**Table 4.1**).

4.4.2 Modified Delphi Results

Overall results of Rounds 1-3 are reported in **Figure 4.2**. Significant consensus statements and priority strategies from the modified Delphi consensus process are presented in **Tables 4.2** and **Table 4.3**. Details from each round are collated in **Tables 4.4** to **4.6**. In Round 1, 38 statements (38/62; 61.3%) across all domains reached consensus. Participants generated an additional nine statements and recommended modification of two additional statements between Round 1 and Round 2. Round 2 included 11 additional participant-generated statements, with a total of 35 statements that were rated. Eighteen statements (18/35; 51.4%)

achieved consensus in Round 2. In Round 3, statements on triggers for antipsychotic medication prescription and antipsychotic minimization and deprescribing activities were ranked as these statements would have the potential to inform practice changes. Perceptions on antipsychotic medication use were not ranked as all healthcare professional perceptions were considered valid. Thirty-one statements on antipsychotic minimization and deprescribing strategies that achieved consensus with a median score of 7–9 from Rounds 1 and 2 were ranked with six statements (6/31; 19.4%) meeting the threshold to be defined as priority statements.

4.4.2.1 Domain 1: Perceptions on Antipsychotic Medication Use

Perceptions of antipsychotic use for the delivery of patient care and patient/staff safety, knowledge and frequency of antipsychotic use, and antipsychotic use guidelines were rated in two rounds. In Round 1, eight statements (8/23; 34.8%) related to participant perceptions on antipsychotic medication use in adult ICU patients with and following critical illness reached consensus (**Table 4.4**). For Round 2, seven new statements were recommended for rating by participants and one statement was modified (informed by participant feedback). In total, 22 statements underwent rating in Round 2 with 13 additional statements reaching consensus (**Table 4.5**). After two rounds of rating, 21 statements out of a total of 30 rated statements reached consensus. Statements reaching consensus focused on perceptions of antipsychotic guidelines and use of antipsychotics in the ICU and on the ward (13/30; 56.5%), perceptions of antipsychotic use for the delivery of patient care and patient/staff safety (4/30; 17.4%), and perceptions on the knowledge and frequency of antipsychotic use (4/30; 17.4%). Two statements reached consensus as non-significant (median 1–3) and the remaining 19 statements were considered significant (median 7–9). Nine statements did not reach consensus after two rounds of rating.

4.4.2.2 Domain 2: Triggers for Antipsychotic Medication Prescription

In Round 1, 14 statements (14/18; 77.8%) related to triggers and clinical indications for antipsychotic medication use in adult patients with and following critical illness reached consensus (**Table 4.4**). For Round 2, one new statement was recommended for rating by participants and one statement was modified based on participant feedback. Eight statements were rated in Round 2 with an additional five statements reaching consensus after Round 2 (**Table 4.5**). After two rounds of rating, 22 statements out of a total of 26 rated statements reached consensus. Statements reaching consensus addressed clinical indications for antipsychotic use (12/26; 46.2%) and the influencing factors informing decision-making for antipsychotic use, prescribing and deprescribing practices (7/26; 26.9%). Three statements reached consensus as non-significant (median 1–3) and the remaining 19 statements were considered significant (median 7–9). Four statements did not reach consensus after two rounds of rating. One participant was identified to have completed Round 1 twice following completion of all consensus rounds. Evaluation of their responses using the mean of their two completed surveys resulted in one statement during Round 1 no longer reaching consensus (i.e., median change from 7 to 6). This statement was subsequently ranked and deemed to be low priority (**Tables 4.4 & 4.6**).

In Round 3, the 19 statements that reached consensus and were significant (median 7–9) in Rounds 1 and 2 were ranked by participant perceived priority (i.e., current clinical practice and perceived beneficial interventions). Three (3/19; 15.8%) reached the threshold for priority (**Table 4.6**). These included statements identifying antipsychotics being used for the clinical indications of hyperactive delirium and patient, family, and/or staff safety (2/3; 66.7%), and not

being able to deliver necessary care and treatment for patients as an important influence on antipsychotic prescribing and deprescribing (1/3; 33.3%).

4.4.2.3 Domain 3: Antipsychotic Minimization and Deprescribing Activities

In Round 1, 16 statements (16/20; 80.0%) related to antipsychotic minimization and deprescribing activities in adult patients with and following critical illness reached consensus (**Table 4.4**). For Round 2, one new statement was recommended for rating by participants. Five statements were rated in Round 2, with no additional statements reaching consensus after Round 2 (**Table 4.5**). Statements reaching consensus addressed current antipsychotic minimization and deprescribing practices (7/20; 35.0%) and potential deprescribing tools and strategies (9/20; 45.0%). All 16 statements were considered significant (median 7–9). Five statements did not reach consensus after two rounds of rating.

In Round 3, the 16 statements that reached consensus and were significant (median 7–9) in Rounds 1 and 2 were ranked by participant perceived priority for clinically effective antipsychotic minimization and deprescribing strategies. Three (3/19; 15.8%) reached the threshold for priority (**Table 4.6**). These included statements recommending ongoing assessment of patients and communication between staff about effectiveness of antipsychotics to help antipsychotic minimization (1/3; 33.3%) and the use of direct communication tools within transfer summaries and additional medication reconciliation at transitions of care as mechanisms to facilitate antipsychotic deprescribing (2/3; 66.7%).

4.5 Discussion

In this National modified Delphi consensus process, we engaged healthcare professionals to determine consensus on three domains related to antipsychotic prescribing (perceptions, current practices, and minimization and deprescribing strategies) for adult patients with and following critical illness. Participant perceptions suggest that antipsychotics are prescribed for three common indications: patient and staff safety, sleep promotion, and clinician concern for team members caring for agitated patients. Further, antipsychotics were perceived to be prescribed more frequently in circumstances where there are resource shortages (e.g., staff availability), high patient volumes, or high work demands. Participants agreed on the importance of the current recommendations related to antipsychotic medication use described in the 2018 Society of Critical Care Medicine Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption [12]. However, participants reported physicians experiencing pressure from other healthcare team members to prescribe antipsychotics. These pressures from other healthcare team members may be influenced by concerns regarding patient and staff safety [33].

Participants prioritized six strategies for consideration when developing and implementing interventions to guide antipsychotic minimization and deprescribing. These strategies focused on limiting antipsychotic prescribing to patients with hyperactive delirium, those patients who are at risk of harm to themselves, their family, and/or staff due to agitation, and those patients where care and treatment are being impacted due to agitation or delirium. Additionally, participant-recommended strategies focused on the need for ongoing assessment of patients, communication between staff supported by direct and efficient communication tools within transfer or discharge summaries, and additional medication reconciliation at transitions of care to identify antipsychotics amenable to deprescribing.

Our study highlights two important considerations related to the development of interventions for antipsychotic minimization and deprescribing in critically ill patients: (1) defining appropriate indications for antipsychotic administration in critically ill patients, and (2) establishing clear verbal and electronic communication mechanisms at transitions of care to address continued antipsychotic prescriptions and to provide discontinuation recommendations. The priority clinical indications identified by participants for antipsychotic medication administration in critically ill patients is consistent with previously reported data on common prescribing indications [34-37]. Antipsychotic medication prescribing in the ICU may at times be necessary due to the challenging clinical circumstances and defining these indications may provide decision-making support for clinicians. Participants identified hyperactive delirium (i.e., agitated delirium) and patient, family, and staff safety as appropriate indications for antipsychotic medication administration. However, additional lower priority clinical indications were identified reflecting current antipsychotic prescribing practices including their use for sleep management, during attempts to wean off intravenous sedation infusions, and when non-pharmacologic interventions for delirium were ineffective. In a recent study characterizing the administration of antipsychotics for sleep management, 36.7% of patients prescribed a medication for sleep management received an antipsychotic medication, particularly when patients were experiencing delirium; these medications were frequently continued at transitions to the hospital ward in this study cohort [13]. Limited data are currently available to advocate for the routine use of antipsychotic medications for these suggested clinical indications. Addressing specific clinical indications where antipsychotic medications should be discouraged may be an important intervention when establishing strategies for antipsychotic minimization.

Participants prioritized the use of communication tools embedded in transfer and discharge summaries as well as additional medication reconciliation to facilitate deprescribing of antipsychotic medications in critically ill patients. Poor communication during patient transitions

of care from the ICU to the hospital ward can lead to medication errors and the continuation of potentially inappropriate medications such as antipsychotics [21, 38]. Communication tools embedded in handoffs at transitions of care are associated with a reduction in medical errors and preventable adverse events.[39] Several systematic reviews identify medication review (i.e., review of current medication list) as an effective tool for short-term drug-related outcome measures (e.g., number of drugs prescribed, adverse drug events) [40-43]. However, in isolation, medication review is likely to be ineffective in improving patient-related outcomes [40, 42, 43]. Medication review in combination with additional tools such as medication reconciliation may be more effective in reducing hospital readmissions in older adults [41]. Medication reconciliation is defined as the deliberate and conscientious interprofessional process of supporting optimal medication management through verification, clarification, and reconciliation of patient's appropriate medication list [23, 44]. Interventions aimed at improving medication reconciliation may address both drug-related and patient-centered outcomes by supporting communication between all healthcare team members in the medication-use process [23]. Computer-enabled tools with automated communication tools and electronic medication reconciliation may offer solutions to reduce medication errors such as inappropriately continued antipsychotic medications [45-47]. It is important to ensure that these communication tools are bidirectional between healthcare professionals to ensure action requests for medication changes or deprescribing are completed [48]. As identified by participants in our study, the merging of bidirectional communication tools with additional purposeful medication reconciliation may provide an effective systematic framework to establish appropriate antipsychotic deprescribing recommendations at transitions of care.

Our study has several strengths. We engaged a diverse group of disciplines in this modified Delphi consensus process including both ward and critical care healthcare professionals (physicians, nurses, and pharmacists) to comprehensively understand and identify

priority considerations for antipsychotic prescribing and deprescribing strategies throughout the course of hospitalization of critically ill adults. Participants were recruited from eight Canadian provinces with representation across all healthcare professional groups, providing diverse perspectives on antipsychotic prescribing practices across Canada. This study also has limitations. First, priorities from healthcare professional groups can broadly vary. To address this limitation, the initial consensus statements were informed by individual interviews and a review of the relevant literature, and we provided free text boxes during each round of the consensus process to refine and strengthen perceptions or statements that may have been missed. Second, completion of all consensus rounds via a virtual format limits discussion between participants and may allow for open interpretation of statements. We provided the opportunity for participants to contact the research team directly if questions regarding interpretation arose. Third, as participants were openly invited to participate, those who completed the consensus process may have different perspectives than those who did not participate. It is possible that some clinically relevant perspectives on how antipsychotics are prescribed or deprescribed were not identified. Lastly, generalizability of the consensus results is limited to a Canadian context where non-pharmacologic interventions for the prevention and management of delirium and agitation are commonplace. The implementation of recommendations from this modified Delphi consensus process assumes the routine utilization of non-pharmacologic strategies for the prevention and management of delirium and agitation of critically ill patients.

4.6 Conclusion

Antipsychotic medications are frequently prescribed in critically ill adult patients to manage symptoms of hyperactive delirium, agitation, and as part of pharmacologic sleep management strategies. This study reports important healthcare professional perceptions on

antipsychotic prescribing practices for the delivery of patient care, knowledge and frequency of antipsychotic use, and perceptions of antipsychotic guidelines and ongoing prescribing at transitions of care. Key healthcare professional stakeholders prioritized evidence-informed strategies to define appropriate clinical indications for antipsychotic medication use in critically ill patients with delirium and agitation and to facilitate inappropriate antipsychotic deprescribing during ICU admission and at transitions of care. These strategies include suggestions on the use of bidirectional communication tools embedded in transfer and discharge summaries as well as additional purposeful medication reconciliation at transitions of care.

4.7 References

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Table 4.1 Participant Characteristics of All Rounds of Modified Delphi Consensus Process

Characteristic	Round 1 (n=57)	Round 2 (n=47)	Round 3 (n=30)
Age category, years			
20-29	1 (1.8%)	1 (2.1%)	0 (0.0%)
30-39	26 (45.6%)	20 (42.6%)	13 (43.3%)
40-49	14 (24.6%)	13 (27.7%)	7 (23.3%)
50-59	9 (15.8%)	8 (17.0%)	6 (20.0%)
60 and above	7 (12.3%)	5 (10.6%)	4 (13.3%)
Sex			
Female	33 (57.9%)	27 (57.4%)	16 (53.3%)
Province			
British Columbia	3 (5.3%)	3 (6.4%)	2 (6.7%)
Alberta	19 (33.3%)	16 (34.0%)	9 (30.0%)
Saskatchewan	3 (5.3%)	3 (6.4%)	1 (3.3%)
Manitoba	1 (1.8%)	1 (2.1%)	1 (3.3%)
Ontario	20 (35.1%)	15 (31.9%)	10 (33.3%)
Quebec	3 (5.3%)	2 (4.3%)	2 (6.7%)
Nova Scotia	5 (8.8%)	4 (8.5%)	2 (6.7%)
New Brunswick	0 (0.0%)	0 (0.0%)	0 (0.0%)
Newfoundland	2 (3.5%)	2 (4.3%)	2 (6.7%)
Prince Edward Island	0 (0.0%)	0 (0.0%)	0 (0.0%)
Territories (Northwest Territories, Nunavut, and Yukon)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Did not answer	1 (1.8%)	1 (2.1%)	1 (3.3%)
Stakeholder Role			
Attending Physician	28 (49.1%)	25 (53.2%)	14 (46.7%)
<i>Clinician administrator</i>	2 (7.1%)	2 (8.0%)	1 (7.1%)
<i>Clinician educator</i>	6 (21.4%)	4 (16.0%)	3 (21.4%)
<i>Clinician scientist</i>	7 (25.0%)	6 (24.0%)	5 (35.7%)
<i>Primary clinician</i>	13 (46.4%)	13 (52.0%)	5 (35.7%)
Licensed Practical Nurse	1 (1.8%)	0 (0.0%)	0 (0.0%)
Nurse Practitioner	2 (3.5%)	2 (4.3%)	1 (3.3%)
Registered Nurse	15 (26.3%)	11 (23.4%)	7 (23.3%)
Pharmacist	9 (15.8%)	8 (17.0%)	7 (23.3%)
Fellow	1 (1.8%)	1 (2.1%)	1 (3.3%)
Resident	1 (1.8%)	0 (0.0%)	0 (0.0%)
Years worked in critical care or hospital environment (median [IQR])	12.0 [6 – 23]	13.0 [7 – 22]	16.0 [9 – 24]

Table 4.2 Summary of Significant Consensus Statements on Perceptions of Antipsychotic Prescribing Practices

<i>Theme 1: Perceptions of antipsychotic use for the delivery of patient care and patient/staff safety</i>
Antipsychotic use improves patient safety (e.g., consider adverse events such as pulling lines, tubes, and drains, falling out of bed, or patients hitting themselves). Antipsychotic use improves staff safety (e.g., reduces physical harm to nurses or doctors). Antipsychotics are commonly used for sleep. The use of antipsychotics provides comfort or decreases stress in the care team (i.e., by calming the patient down), irrespective of whether the underlying cause of delirium is treated.
<i>Theme 2: Perceptions of the knowledge and frequency of antipsychotic use</i>
Antipsychotics are prescribed more frequently when there are resource shortages (e.g., number of physical restraints available, staff available for patient monitoring), high patient volume, and high work demands. Long-standing practices influence the decision to prescribe an antipsychotic (i.e., prescribing an antipsychotic has been done for the past 15-20 years, creating an “institutional inertia”). Antipsychotics do not treat delirium, but rather shift patients from a state of hyperactive delirium to hypoactive delirium.
<i>Theme 3: Perception of antipsychotic guidelines and use of antipsychotics in the ICU and on the ward</i>
Antipsychotic prescribing practices are inconsistent with current professional society guidelines on indications for antipsychotic medication use. Typically, antipsychotics are used more in the ICU than on the ward. The type of antipsychotic prescribed (i.e., typical vs. atypical) differs depending on the culture of the unit. Culture within the ICU and ward (e.g., ideally all patients are calm and sleeping at night) contributes to antipsychotic prescribing practices. Antipsychotic medications should be considered for treating delirium compared to alternative pharmacological therapies for delirium, such as benzodiazepines. The prescribing and use of antipsychotics differs between day and night shifts. Antipsychotic prescriptions are generally continued, despite lack of clinical indication for their ongoing appropriate use. The short-term benefits of the effects of antipsychotics are often the focus for their use or are considered of higher importance than potential long-term consequences. There is a pervasive perception amongst staff that the use of antipsychotics for treating delirium is guided by strong evidence. The risk-benefit ratio of antipsychotic prescribing and use is rarely discussed with the substitute decision maker for informed consent. Current professional society guidelines outlining recommendations on when antipsychotic medication should be used are not generally agreed upon amongst staff.

Other ICU care team members put pressure on the attending physician to prescribe antipsychotics, which influences prescribing practices.

Table 4.3 Prioritized Strategies for Antipsychotic Minimization and Deprescribing

Item	Theme Mean (SD)	Item Mean (SD)
Theme 4: Clinical indications for antipsychotic use		
Antipsychotics should be used for hyperactive delirium (i.e., agitated delirium) treatment and management.	11.1 (3.3)	15.5 (18.1)
Antipsychotics should be used when patient, family and/or staff safety (e.g., pulling tubes, falling out of bed, physical aggression, etc.) is at risk.		17.4 (8.7)
Theme 5: Influences on decision-making for antipsychotic use, prescribing and deprescribing practices		
Antipsychotics are prescribed when necessary care for the patient and treatment are being impacted (i.e., due to agitation, delirium, etc.).	16.7 (2.6)	20.6 (11.2)
Theme 6: Current practices for antipsychotic minimization and deprescribing		
Ongoing assessment of the patient and communication between staff about the effectiveness of the treatment (including qualitative feedback) helps to minimize antipsychotic use and promote deprescribing.	14.3 (4.1)	21.8 (14.7)
Theme 7: Deprescribing tools and strategies		
There is a need for a direct and efficient communication tool within transfer or discharge summaries between prescribers at transitions of care to identify continued medications such as antipsychotics and to provide discontinuation recommendations.	11.1 (3.5)	16.1 (8.3)
Additional medication reconciliation should occur at transitions of care to identify antipsychotics that have been continued without a clear ongoing clinical indication.		15.1 (9.6)

Statements defined to have priority if the statement's mean ranking from all participants was equal to or greater than one standard deviation above the theme's mean ranking ensuring that themes with unequal numbers of statements were equalized

Table 4.4 Round 1 Likert Scale Results from Participant Rating Responses

<i>Theme 1: Perceptions of antipsychotic use for the delivery of patient care and patient/staff safety</i>	Median	Decision
1. Antipsychotic use improves patient safety (e.g., consider adverse events such as pulling lines, tubes and drains, falling out of bed, or patients hitting themselves).	6	NON-CONSENSUS
2. Antipsychotic use improves staff safety (e.g., reduces physical harm to nurses or doctors).	6	NON-CONSENSUS
3. Patient compliance with daily care is safer or easier when chemical restraints, such as antipsychotics, are used.	5	NON-CONSENSUS
4. Antipsychotics improve patient sleep.	4	NON-CONSENSUS
5. When antipsychotic medications are avoided in patients with delirium or agitation, there are delays in therapy (e.g., mobilization, diagnostic tests, etc.).	5	NON-CONSENSUS
6. When antipsychotic medications are used, there are delays in therapy (e.g., neurological exams) and participation in care.	5	NON-CONSENSUS
7. When antipsychotic medications are avoided, there is an increase in symptoms of family distress.	6	NON-CONSENSUS
8. The use of antipsychotics provides comfort or decreases stress in the care team (i.e., by calming the patient down), irrespective of whether the underlying cause of delirium is treated.	6	NON-CONSENSUS
<i>Theme 2: Perceptions of the knowledge and frequency of antipsychotic use</i>		
1. Antipsychotics are only used for severe and significant agitation or aggression that is putting either the patient or others at risk.	5	NON-CONSENSUS
2. Antipsychotics are not helpful for agitation.	3	CONSENSUS
3. Antipsychotics are prescribed more frequently when there are resource shortages (e.g., number of physical restraints available, staff available for patient monitoring), high patient volume, and high work demands.	5	NON-CONSENSUS
4. Long-standing practices influence the decision to prescribe an antipsychotic (i.e., prescribing an antipsychotic has been done for the past 15-20 years, creating an “institutional inertia”).	7	CONSENSUS
5. Antipsychotics do not treat delirium, but rather shift patients from a state of hyperactive delirium to hypoactive delirium.	7	CONSENSUS
6. Staff feel confident and empowered to deprescribe antipsychotic medications.	4	NON-CONSENSUS
<i>Theme 3: Perception of antipsychotic guidelines and use of antipsychotics in the ICU and on the ward</i>		
1. Antipsychotic prescribing practices are inconsistent with current professional society guidelines on indications for antipsychotic medication use.	6	NON-CONSENSUS
2. Typically, antipsychotics are used more in the ICU than on the ward.	7	CONSENSUS
3. The type of antipsychotic prescribed (i.e., typical vs. atypical)	7	CONSENSUS

differs depending on the culture of the unit.		
4. Culture within the ICU and ward (e.g., ideally all patients are calm and sleeping at night) contributes to antipsychotic prescribing practices.	7	CONSENSUS
5. Antipsychotics are preferred in comparison to continuous sedation because they have safer sedation effects.	5	NON-CONSENSUS
6. Antipsychotic medications should be considered for treating delirium compared to alternative pharmacological therapies for delirium, such as benzodiazepines.	7	CONSENSUS
7. The prescribing and use of antipsychotics differs between day and night shifts.	6	NON-CONSENSUS
8. Antipsychotic prescriptions are generally continued, despite lack of clinical indication for their ongoing appropriate use.	6	NON-CONSENSUS
9. The short-term benefits of the effects of antipsychotics are often the focus for their use or are considered of higher importance than potential long-term consequences.	7	CONSENSUS
Theme 4: Clinical indications for antipsychotic use		
1. Antipsychotics should be used for hyperactive delirium (i.e., agitated delirium) treatment and management.	7	CONSENSUS
2. Antipsychotics should be used for hypoactive delirium treatment and management.	2	CONSENSUS
3. Antipsychotics should be used when non-pharmacological interventions for delirium are ineffective.	7	CONSENSUS
4. Antipsychotics should be used when patient, family and/or staff safety (e.g., pulling tubes, falling out of bed, physical aggression, etc.) is at risk.	8	CONSENSUS
5. Antipsychotics are the “path of least resistance” when dealing with patients who are agitated or experiencing hyperactive delirium, compared to physical restraints.*	6	CONSENSUS
6. Antipsychotics help to re-establish day and night routines or mitigate sleep disturbances.	4	NON-CONSENSUS
7. Environmental stressors (i.e., lack of windows, frequent noise, lights on during the night, patient isolation, and intrusive treatment) promote increased prescribing of antipsychotics.	8	CONSENSUS
8. Antipsychotics are useful when weaning agitated patients off of sedation.	6	NON-CONSENSUS
9. Antipsychotics are useful for the management of alcohol withdrawal.	3	CONSENSUS
10. Antipsychotics are useful to help achieve patient sedation.	5	NON-CONSENSUS
11. Antipsychotics are useful for managing symptoms of patient anxiety and panic.	5	NON-CONSENSUS
12. Antipsychotics are often prescribed for their side effects (e.g., sleep) rather than their main effect.	7	CONSENSUS
Theme 5: Influences on decision-making for antipsychotic use, prescribing and deprescribing practices		
1. The decision to prescribe an antipsychotic depends on team opinions regarding antipsychotic use during rounds.	7	CONSENSUS
2. There is not a clear understanding of clinical practice	7	CONSENSUS

guidelines for antipsychotic medication use in the ICU and on the ward.		
3. Antipsychotics are prescribed when staff advocates for antipsychotics to make care for the patient easier.	7	CONSENSUS
4. Antipsychotics are prescribed when necessary care for the patient and treatment are being impacted (i.e., due to agitation, delirium, etc.).	7	CONSENSUS
5. Staff who evaluate a patient's records are missing information or do not have the history on the patient and why the antipsychotic was prescribed. Without this history, staff assume that the antipsychotic is necessary rather than weaning the patient off the medication.	6	NON- CONSENSUS
6. Healthcare utilization costs (e.g., length of stay) plays an important role when deciding to prescribe an antipsychotic.	3	CONSENSUS
7. When a patient is transferred from the ICU, insufficient information about the use of antipsychotics in the ICU generates uncertainty about the continuation of antipsychotics and so patients often remain on antipsychotics due to this missing information.	7	CONSENSUS
Theme 6: Current practices for antipsychotic minimization and deprescribing		
1. Weekend discharges impact the ability to effectively deprescribe antipsychotics.	5	NON- CONSENSUS
2. Antipsychotic prescribing occurs most often during night shifts.	5	NON- CONSENSUS
3. Antipsychotic deprescribing frequently occurs during transitions of care (i.e., ICU to ward, ICU to home, ward to home).	6	NON- CONSENSUS
4. Ongoing assessment of the patient and communication between staff about the effectiveness of the treatment (including qualitative feedback) helps to minimize antipsychotic use and promote deprescribing.	7	CONSENSUS
5. There is a lack of decision-making support tools or policies to guide antipsychotic deprescribing practices.	7	CONSENSUS
6. There is insufficient communication at transitions of care regarding current medications and deprescribing.	7	CONSENSUS
7. Family presence and engagement facilitates antipsychotic minimization or deprescribing of antipsychotics.	7	CONSENSUS
8. Non-pharmacologic interventions assist in antipsychotic minimization.	8	CONSENSUS
9. Non-pharmacologic interventions as a strategy for antipsychotic minimization are not a PRIORITY compared to other focuses (i.e., other aspects of patient care and treatment).	7	CONSENSUS
10. Non-pharmacologic intervention experts (e.g., geriatricians) help to facilitate deprescribing of antipsychotics.	7	CONSENSUS
11. Deprescribing antipsychotics is not feasible at transitions of care (from ICU to ward) when the patient is still delirious.	5	NON- CONSENSUS
Theme 7: Deprescribing tools and strategies		

1. There is a need for a direct and efficient communication tool within transfer or discharge summaries between prescribers at transitions of care to identify continued medications such as antipsychotics and to provide discontinuation recommendations.	8	CONSENSUS
2. There is a need for additional antipsychotic medication prescribing accountability to facilitate deprescribing (e.g., automatic stop dates, no “as needed” dosing allowed, force function alerts, flags for review, and reassessment dates).	8	CONSENSUS
3. Additional medication reconciliation should occur at transitions of care to identify antipsychotics that have been continued without clear ongoing clinical indication.	8	CONSENSUS
4. Formal education sessions on indications for antipsychotic medication prescribing and deprescribing are needed.	9	CONSENSUS
5. There is a need for expert consultations on medication management upon transitions of care (e.g., geriatrics consultation, ward follow-up, and outpatient follow-up).	7	CONSENSUS
6. There is a need for the creation of pharmacist-driven deprescribing strategies or algorithms.	8	CONSENSUS
7. There is a need for tapering protocols and discharge medication care bundles.	8	CONSENSUS
8. There is a need for policy development on antipsychotic prescribing practices.	8	CONSENSUS
9. There should be practice audits for feedback to prescribers on antipsychotic prescribing practices with non-punitive mechanisms.	8	CONSENSUS

* One participant was identified to have completed Round 1 twice following completion of all consensus rounds. Evaluation with their responses using the mean of their two completed surveys resulted in this statement no longer reaching consensus (i.e., median change from 7 to 6). This statement was subsequently ranked and deemed to be low priority.

Table 4.5 Round 2 Likert Scale Results from Participant Rating Responses

<i>Theme 1: Perceptions of antipsychotic use for the delivery of patient care and patient/staff safety</i>	Median	Decision
1. Antipsychotic use improves patient safety (e.g., consider adverse events such as pulling lines, tubes and drains, falling out of bed, or patients hitting themselves).	7	CONSENSUS
2. Antipsychotic use improves staff safety (e.g., reduces physical harm to nurses or doctors).	7	CONSENSUS
3. Patient compliance with daily care is safer or easier when chemical restraints, such as antipsychotics, are used.	6	NON-CONSENSUS
4. Antipsychotics are commonly used for sleep.**	8	CONSENSUS
5. When antipsychotic medications are avoided in patients with delirium or agitation, there are delays in therapy (e.g., mobilization, diagnostic tests, etc.).	5	NON-CONSENSUS
6. When antipsychotic medications are used in patients with delirium or agitation, there are delays in therapy (e.g., neurological exams) and participation in care.	5	NON-CONSENSUS
7. When antipsychotic medications are avoided, there is an increase in families experiencing symptoms of distress.	6	NON-CONSENSUS
8. The use of antipsychotics provides comfort or decreases stress in the care team (i.e., by calming the patient down), irrespective of whether the underlying cause of delirium is treated.	7	CONSENSUS
9. Chemical restraints, such as antipsychotics, are a gentler form of restraint and are better tolerated by patients, as opposed to physical restraints.*	6	NON-CONSENSUS
10. Staff may be reluctant to administer antipsychotics due to lack of knowledge regarding the value of antipsychotics.*	4	NON-CONSENSUS
<i>Theme 2: Perceptions of the knowledge and frequency of antipsychotic use</i>		
1. Antipsychotics are only used for severe and significant agitation or aggression that is putting either the patient or others at risk.	6	NON-CONSENSUS
2. Antipsychotics are prescribed more frequently when there are resource shortages (e.g., number of physical restraints available, staff available for patient monitoring), high patient volume, or high work demands.	7	CONSENSUS
3. Staff feel confident and empowered to deprescribe antipsychotic medications.	4	NON-CONSENSUS
<i>Theme 3: Perception of antipsychotic guidelines and use of antipsychotics in the ICU and on the ward</i>		
1. Antipsychotic prescribing practices are inconsistent with current professional society guidelines on indications for antipsychotic medication use.	7	CONSENSUS
2. Antipsychotics are preferred in comparison to continuous sedation because they have safer sedation effects.	5	NON-CONSENSUS
3. The prescribing and use of antipsychotics differs between day and night shifts.	8	CONSENSUS

4. Antipsychotic prescriptions are generally continued, despite lack of clinical indication for their ongoing appropriate use.	7	CONSENSUS
5. There is a pervasive perception amongst staff that the use of antipsychotics for treating delirium is guided by strong evidence.*	7	CONSENSUS
6. The risk-benefit ratio of antipsychotic prescribing and use is rarely discussed with the substitute decision maker for informed consent.*	8	CONSENSUS
7. Current professional society guidelines outlining recommendations on when antipsychotic medication should be used are not generally agreed upon amongst staff.*	7	CONSENSUS
8. Current professional society guidelines on antipsychotic medication use are informed by high quality evidence and provide meaningful clinical guidance on when antipsychotics should or should not be prescribed.*	3	CONSENSUS
9. Other ICU care team members put pressure on the attending physician to prescribe antipsychotics, which influences prescribing practices.*	7	CONSENSUS
Theme 4: Clinical indications for antipsychotic use		
1. Antipsychotics help to re-establish day and night routines or mitigate sleep disturbances.	5	NON-CONSENSUS
2. Antipsychotics are useful for the management of alcohol withdrawal.**	3	CONSENSUS
3. Antipsychotics are useful to help achieve patient sedation.	6	NON-CONSENSUS
4. Antipsychotics are useful for managing symptoms of patient anxiety and panic.	5	NON-CONSENSUS
5. Antipsychotics are safe for all ICU patients.*	2	CONSENSUS
6. Antipsychotic medications are used to avoid the use of continuous IV sedative infusions with hyperactive delirium or agitation.	7	CONSENSUS
7. Antipsychotics are used to manage the symptoms of agitation or hyperactive delirium when there is an inability to modify certain underlying medical drivers responsible for patient illness (e.g., exposure to medically necessary medications that increase the risk of delirium).	8	CONSENSUS
Theme 5: Influences on decision-making for antipsychotic use, prescribing and deprescribing practices		
1. Staff who evaluate a patient's records may be missing information, do not have the history on the patient, or the confidence (e.g., junior staff) to question why the antipsychotic was prescribed. Therefore, staff assume that the antipsychotic is necessary rather than weaning the patient off the medication.	7	CONSENSUS
Theme 6: Current practices for antipsychotic minimization and deprescribing		
1. Weekend discharges impact the ability to effectively deprescribe antipsychotics.	5	NON-CONSENSUS
2. Antipsychotic prescribing occurs most often during night shifts.	5	NON-CONSENSUS

3. Antipsychotic deprescribing frequently occurs during transitions of care (i.e., ICU to ward, ICU to home, ward to home).	6	NON- CONSENSUS
4. Deprescribing antipsychotics is not feasible at transitions of care (from ICU to ward) when the patient is still delirious.	5	NON- CONSENSUS
Theme 7: Deprescribing tools and strategies		
1. There is a need for an informed consent process and documentation for antipsychotic use and administration.*	5	NON- CONSENSUS

Note: Participants were asked to provide additional feedback and/or suggest missing items for ranking in subsequent rounds. *Indicates new item added after the first round. **Indicates modified items after the first round.

Table 4.6 Round 3 Weighted Ranking Results from Participant Responses

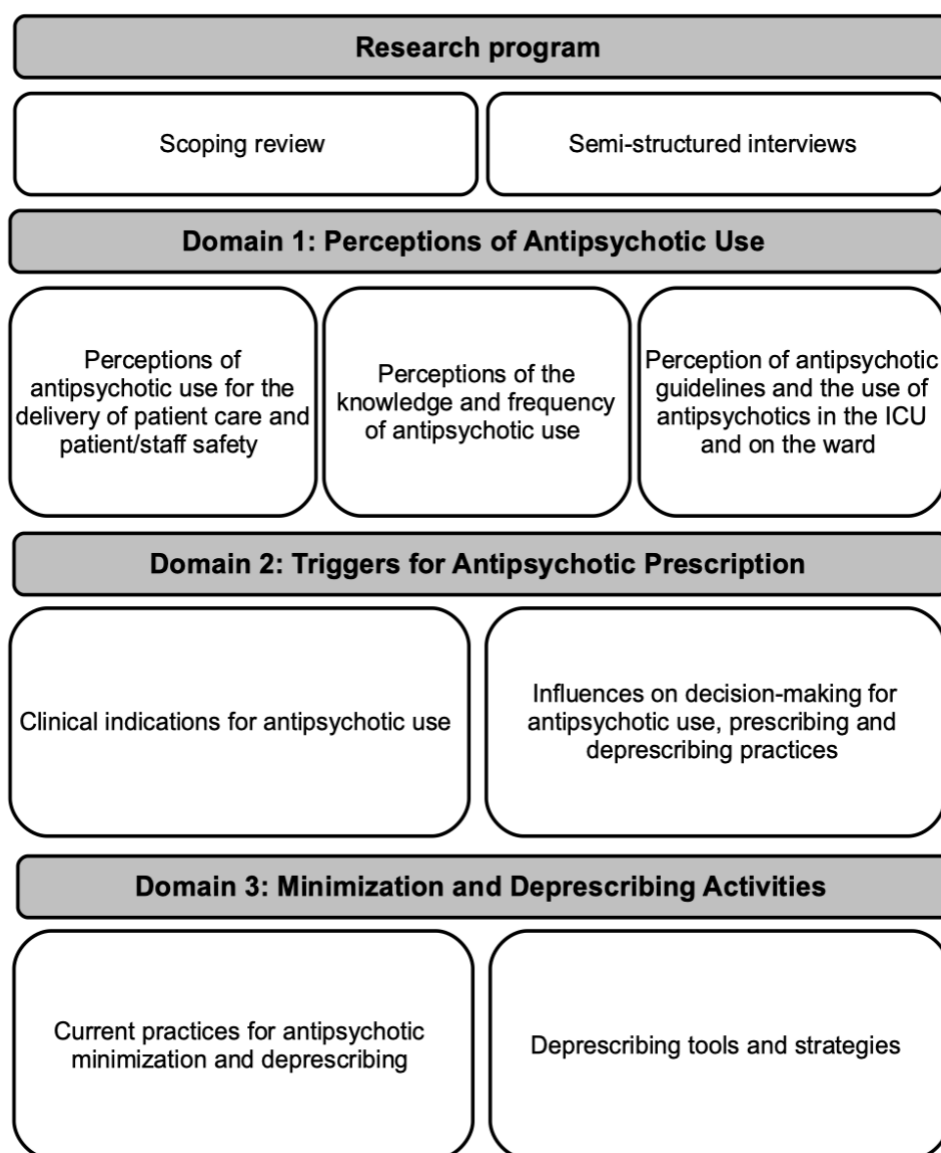
Item	Theme Mean (SD)	Item Mean (SD)	Decision
Theme 4: Clinical indications for antipsychotic use			
Antipsychotics should be used for hyperactive delirium (i.e., agitated delirium) treatment and management.	11.1 (3.3)	15.5 (18.1)	PRIORITY
Antipsychotics should be used when non-pharmacological interventions for delirium are ineffective.		11.2 (8.5)	NON-PRIORITY
Antipsychotics should be used when patient, family and/or staff safety (e.g., pulling tubes, falling out of bed, physical aggression, etc.) is at risk.		17.4 (8.7)	PRIORITY
Antipsychotics are the path of least resistance when dealing with patients who are agitated or experiencing hyperactive delirium, compared to physical restraints.*		8.6 (8.3)	NON-PRIORITY
Environmental stressors (e.g., lack of windows, frequent noise, lights on during the night, patient isolation, and intrusive treatment) promote increased prescribing of antipsychotics.		8.5 (5.2)	NON-PRIORITY
Antipsychotics are useful when weaning agitated patients off of sedation.		8.7 (6.8)	NON-PRIORITY
Antipsychotics are often prescribed for their side effects (e.g., sleep) rather than their main effect.		8.1 (8.8)	NON-PRIORITY
Antipsychotic medications are used to avoid the use of continuous intravenous sedative infusions with hyperactive delirium or agitation.		11.3 (9.9)	NON-PRIORITY
Antipsychotics are used to manage the symptoms of agitation or hyperactive delirium when there is an inability to modify certain underlying medical drivers responsible for patient illness (e.g., exposure to medically necessary medications that increase the risk of delirium).		10.6 (9.1)	NON-PRIORITY
Theme 5: Influences on decision-making for antipsychotic use, prescribing and deprescribing practices			
The decision to prescribe an antipsychotic depends on team opinions regarding antipsychotic use during rounds.	16.7 (2.6)	19.0 (9.4)	NON-PRIORITY
There is not a clear understanding of clinical practice guidelines for antipsychotic		14.9 (7.0)	NON-PRIORITY

medication use in the ICU and on the ward.			
Antipsychotics are prescribed when staff advocates for antipsychotics to make care for the patient easier.		16.6(8.8)	NON-PRIORITY
Antipsychotics are prescribed when necessary care for the patient and treatment are being impacted (i.e., due to agitation, delirium, etc.).		20.6 (11.2)	PRIORITY
When a patient is transferred from the ICU, insufficient information about the use of antipsychotics in the ICU generates uncertainty about the continuation of antipsychotics and so patients often remain on antipsychotics due to this missing information.		14.2 (8.0)	NON-PRIORITY
Staff who evaluate a patient's records may be missing information, do not have the history on the patient, or the confidence (e.g., junior staff) to question why the antipsychotic was prescribed. Therefore, staff assume that the antipsychotic is necessary rather than weaning the patient off the medication.		14.8 (7.3)	NON-PRIORITY
Theme 6: Current practices for antipsychotic minimization and deprescribing			
Ongoing assessment of the patient and communication between staff about the effectiveness of the treatment (including qualitative feedback) helps to minimize antipsychotic use and promote deprescribing.	14.3 (4.1)	21.8 (14.7)	PRIORITY
There is a lack of decision-making support tools or policies to guide antipsychotic deprescribing practices.		14.6 (7.7)	NON-PRIORITY
There is insufficient communication at transitions of care regarding current medications and deprescribing.		13.2 (9.0)	NON-PRIORITY
Family presence and engagement facilitates antipsychotic minimization or deprescribing of antipsychotics.		12.9 (6.3)	NON-PRIORITY
Non-pharmacological interventions assist in antipsychotic minimization.		17.2 (10.4)	NON-PRIORITY
Non-pharmacological interventions as a strategy for antipsychotic minimization are not a PRIORITY compared to other focuses (i.e., other aspects of patient care and treatment).		10.4 (7.0)	NON-PRIORITY
Non-pharmacological intervention experts (e.g., geriatricians) help to facilitate deprescribing of antipsychotics.		10.0 (9.4)	NON-PRIORITY
Theme 7: Deprescribing tools and strategies			
There is a need for a direct and efficient communication tool within transfer or	11.1 (3.5)	16.1 (8.3)	PRIORITY

discharge summaries between prescribers at transitions of care to identify continued medications such as antipsychotics and to provide discontinuation recommendations.			
There is a need for additional antipsychotic medication prescribing accountability to facilitate deprescribing (e.g., automatic stop dates, as needed dosing allowed, force function alerts, flags for review, and reassessment dates).		12.6 (7.7)	NON-PRIORITY
Additional medication reconciliation should occur at transitions of care to identify antipsychotics that have been continued without clear ongoing clinical indication.		15.1 (9.6)	PRIORITY
Formal education sessions on indications for antipsychotic medication prescribing and deprescribing are needed.		8.1 (5.4)	NON-PRIORITY
There is a need for expert consultations on medication management upon transitions of care (e.g., geriatrics consultation, outpatient follow-up).		6.8 (6.9)	NON-PRIORITY
There is a need for the creation of pharmacist-driven deprescribing strategies or algorithms.		14.1 (10.6)	NON-PRIORITY
There is a need for tapering protocols and discharge medication care bundles.		10.1 (7.5)	NON-PRIORITY
There is a need for policy development on antipsychotic prescribing practices.		9.1 (6.4)	NON-PRIORITY
There should be practice audits for feedback to prescribers on antipsychotic prescribing practices with non-punitive mechanisms.		7.9 (5.6)	NON-PRIORITY

* One participant was identified to have completed Round 1 twice following completion of all consensus rounds. Evaluation with their responses using the mean of their two completed surveys resulted in this statement no longer reaching consensus (i.e., median change from 7 to 6). This statement was subsequently ranked and deemed to be low priority.

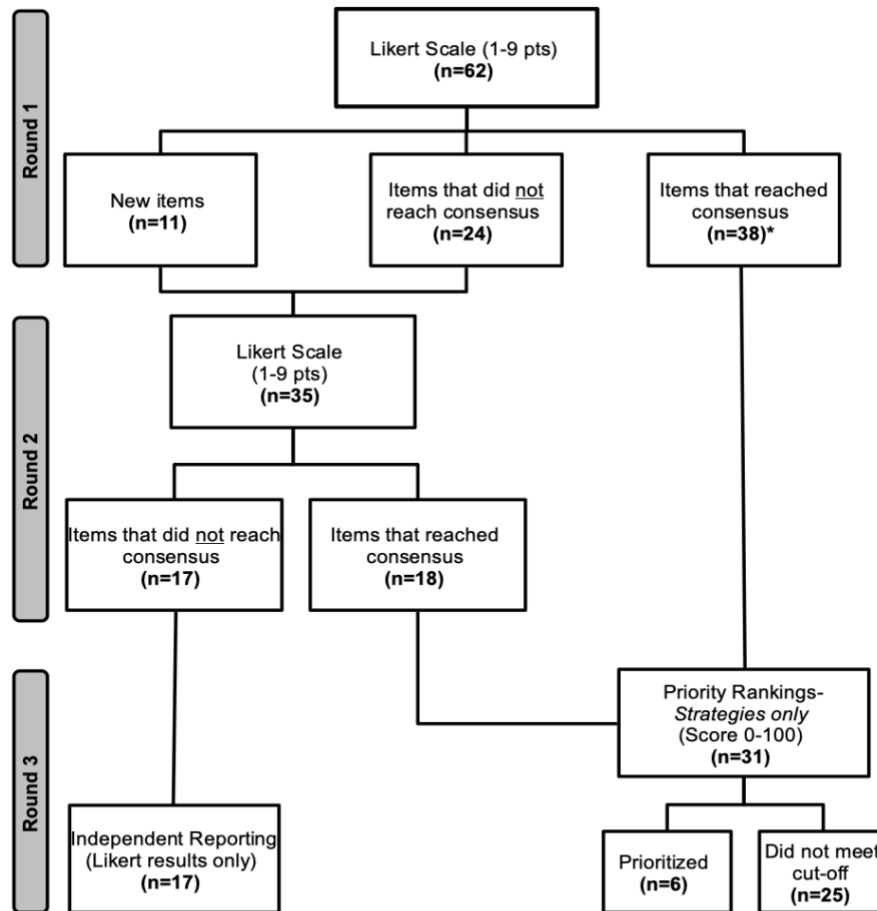
Figure 4.1 Research Program Overview Informing the Modified Delphi Consensus



Process¹

¹The results of the research program generated three domains and seven themes evaluated during the survey rounds

Figure 4.2 Overview of the Results from the Modified Delphi Consensus Process for Perceptions on Antipsychotic Prescribing Practices and Antipsychotic Minimization and Deprescribing Strategies



Rated statements must have achieved a median score of 1-3 or 7-9 to reach consensus. Priority ranked statements were determined to be priority strategies if their mean score was greater than the theme mean score plus one standard deviation.

* One participant was identified to have completed Round 1 twice following completion of all consensus rounds. Evaluation with their responses using the mean of their two completed surveys resulted in this statement no longer reaching consensus (i.e., median change from 7 to 6). This statement was subsequently ranked and deemed to be low priority.

Appendix 4.1 Conducting and REporting and DElphi Studies (CREDES) Checklist

Items of reporting	Reported on page
<i>Purpose and rationale.</i> The purpose of the study should be clearly defined and demonstrate the appropriateness of the use of the Delphi technique as a method to achieve the research aim. A rationale for the choice of the Delphi technique as the most suitable method needs to be provided.	5
<i>Expert panel.</i> Criteria for the selection of experts and transparent information on recruitment of the expert panel, sociodemographic details including information on expertise regarding the topic in question, (non)response and response rates over the ongoing iterations should be reported.	5-6, 8, Table 4.1
<i>Description of the methods.</i> The methods employed need to be comprehensible; this includes information on preparatory steps (How was available evidence on the topic in question synthesized?), piloting of material and survey instruments, design of the survey instrument(s), the number and design of survey rounds, methods of data analysis, processing and synthesis of experts' responses to inform the subsequent survey round and methodological decisions taken by the research team throughout the process.	5 - 8
<i>Procedure.</i> Flow chart to illustrate the stages of the Delphi process, including a preparatory phase, the actual 'Delphi rounds', interim steps of data processing and analysis, and concluding steps.	Figure 4.1, Figure 4.2
<i>Definition and attainment of consensus.</i> It needs to be comprehensible to the reader how consensus was achieved throughout the process, including strategies to deal with non-consensus.	7-8
<i>Results.</i> Reporting of results for each round separately is highly advisable in order to make the evolving of consensus over the rounds transparent. This includes figures showing the average group response, changes between rounds, as well as any modifications of the survey instrument such as deletion, addition or modification of survey items based on previous rounds.	8 - 12

<i>Discussion of limitations.</i> Reporting should include a critical reflection of potential limitations and their impact of the resulting guidance.	16
<i>Adequacy of conclusions.</i> The conclusions should adequately reflect the outcomes of the Delphi study with a view to the scope and applicability of the resulting practice guidance.	17
<i>Publication and dissemination.</i> The resulting guidance on good practice should be clearly identifiable from the publication, including recommendations for transfer into practice and implementation. If the publication does not allow for a detailed presentation of either the resulting practice guidance or the methodological features of the applied Delphi technique, or both, reference to a more detailed presentation elsewhere should be made (e.g. availability of the full guideline from the authors or online; publication of a separate paper reporting on methodological details and particularities of the process (e.g. persistent disagreement and controversy on certain issues)). A dissemination plan should include endorsement of the guidance by professional associations and health care authorities to facilitate implementation.	15

Appendix 4.2 Antipsychotic Delphi Round 1 Questionnaire: Likert Scale Rating of Consensus Statements

I: Introduction

Dear colleagues,

Thank you for agreeing to participate in this survey addressing experiences with antipsychotic prescribing and administration practices and evaluating facilitators and barriers to antipsychotic medication prescribing and deprescribing in patients who are experiencing critical illness or have transitioned to the hospital ward following critical illness.

In the first phases of this study, we conducted interviews with critical care and ward physicians, nurses, and pharmacists to better understand antipsychotic prescribing practices within the ICU and on the ward for patients initially admitted with critical illness. Participants were asked about their perspectives on prescribing as well as facilitators and barriers to antipsychotic medication deprescribing during patient hospitalization. We further reviewed the literature with a scoping review on perceptions related to antipsychotic prescribing practices in acute care settings.

In this survey, you will be asked to rank a series of experiences, facilitators, and barriers from these interviews and a scoping review conducted by our team on a 9-point Likert scale where 1 reflects “strongly disagree” and 9 reflects “strongly agree”. You can select any whole-point score on this scale that best represents your perspective. At the end of each section, you will be presented with a free-text box to suggest any experiences or practices that you think are missing. Participant-suggested items will be included in subsequent rounds for consideration. At the end of the survey, you will be asked a series of demographic questions. Your information will be held in strict confidence and will only be used for aggregate reporting. **We anticipate this survey to take approximately 20 minutes to complete.** You may save your responses and return to the survey at any time before **February 4th, 2022 at 4pm MST**. You will receive a summary of the results of this survey by email after the survey closes.

By completing this survey, you are providing implied consent to participate. This study has been approved by the University of Calgary Conjoint Health Research Ethics Board (REB-21-0963). A copy of the implied consent form is included in the survey link below.

Follow this link to the survey: _____

We greatly appreciate your time and the contribution of your expertise to this research study. If you have any questions about this study, please contact Dr. Kirsten Fiest (kmfiest@ucalgary.ca) or Dr. Natalia Jaworska (njaworsk@ucalgary.ca).

Sincerely,
Dr. Natalia Jaworska, MD, MSc, FRCPC
University of Calgary
Department of Critical Care Medicine

II: Implied Consent



**UNIVERSITY OF CALGARY
IMPLIED CONSENT TO PARTICIPATE IN RESEARCH**

TITLE: Facilitators and barriers to deprescribing antipsychotic medications in critically ill adult patients at transitions of care: A mixed methods study

SPONSOR: None.

FUNDER: This study is unfunded.

INVESTIGATORS: Dr. Natalia Jaworska, Dr. Kirsten M. Fiest

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INTRODUCTION

Dr. Kirsten Fiest and associates from the Department of Critical Care Medicine at the University of Calgary are conducting a research study.

This consent form is only part of the process of informed consent. It should give you the basic idea of what the research is about and what your participation will involve. If you would like more detail about something mentioned here, or information not included here, please ask. Take the time to read this carefully and to understand any accompanying information.

You were identified as a possible participant in this study because you are a hospital ward or critical care physician, nurse, or pharmacist who works with either critically ill patients or those following critical illness who receive antipsychotic medications. Your participation in this research study is voluntary.

Antipsychotic medications are commonly prescribed for critically ill patients. Up to 42% of patients receive an antipsychotic in the intensive care unit (ICU). These antipsychotic medications are prescribed for various reasons but are typically prescribed for the symptoms of delirium. Randomized studies show antipsychotics do not alter the course of delirium. Long-term use is associated with increased sudden death, falls, and cognitive impairment. Still, one third of patients prescribed antipsychotics in the ICU will go home with an ongoing prescription without a clinical indication. Limited literature is available to understand the factors, facilitators, and barriers that influence antipsychotic prescribing and deprescribing practices in patients following critical illness.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to understand the factors that influence antipsychotic medication prescribing and administration practices of critical care and ward healthcare providers (physicians, nurses, and pharmacists) in patients with or following critical illness, and to identify facilitators and barriers to deprescribing antipsychotic medication in adult patients following critical illness in the ICU and during hospitalization. The goal of the survey is to gain consensus on healthcare provider experiences and identified facilitators and barriers to antipsychotic deprescribing through repeated rounds of surveys.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 20 to 30 people will take part in this study Canada wide. Approximately 10 people will take part in this study through the University of Calgary.

WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY?

If you volunteer to participate in this study, the researcher will ask you to do the following: Complete multiple rounds of surveys (expect two to three), rating from 1 to 9, experiences related to antipsychotic prescribing practices as well as facilitators and barriers to antipsychotic medication deprescribing for critically ill patients and those patients who have moved from the ICU to the hospital ward.

Each round of surveys should take no more than 20 minutes to complete.

Surveys will occur approximately every 3 weeks during which you will have 2 weeks to complete the survey.

ARE THERE ANY POTENTIAL RISKS OR DISCOMFORTS THAT I CAN EXPECT FROM THIS STUDY?

There are no risks associated with your participation.

HOW LONG WILL I BE IN THIS STUDY?

You will be in this study for approximately 6 to 9 weeks during which you will be asked to complete and anticipated 2 to 3 surveys in at approximately 3-week intervals. You may be asked to extend your time in the study or complete additional rounds of surveys if consensus cannot be achieved on items with the previously completed surveys.

ARE THERE ANY POTENTIAL BENEFITS IF I PARTICIPATE?

If you agree to take part in this study, there may or may not be a direct benefit to you. By choosing to take part, you will have the opportunity to provide data to develop an understanding of antipsychotic medication prescribing practices for patients with or following critical illness.

CAN I STOP BEING IN THE STUDY?

Your participation in this study is entirely voluntary. You may withdraw from the study at any time by closing the web browser or not completing the survey. Should you choose to withdraw from the study, your data can only be removed up until the point of submission of their responses to the survey, after which data cannot be removed.

As contact information is not collected from participants, following submission of the survey your data will not be linked to you and may be impossible to extract.

Please note, although on request your data may be withdrawn from the study analyses, your raw data will be kept for the minimum required data retention interval of 5 years.

WILL INFORMATION ABOUT ME AND MY PARTICIPATION BE KEPT CONFIDENTIAL?

The researchers will do their best to make sure that your private information is kept confidential. Information about you will be handled as confidentially as possible, but there is always the potential for an unintended breach of privacy. The research team will handle data according to the Data Management Plan as outlined below:

The surveys will be administered through Qualtrics. Qualtrics is an online survey platform with servers located in Toronto, Ontario, Canada. All data are encrypted and stored directly on its servers. Researcher access to the survey data is password-protected and the transmission is encrypted. Survey responses cannot be linked to your computer.

No identifiable information about you will be kept with the research data.

All research data and records will be stored electronically on a secure network with password protection.

Only members of the research team will have access to your research records.

Use of the data collected may include academic presentations or papers.

Any writings, publications, or presentations of the data collected will not include any personal identifying information that could link the data to any participating individual.

The study investigators will make every effort to maintain the confidentiality of your research records, to the extent permitted by law (e.g., disclosed child abuse or neglect must be reported) and legal requests (e.g., court applications seeking disclosure of research data are possible). The University of Calgary Conjoint Health Research Ethics Board will have access to the records.

HOW LONG WILL INFORMATION FROM THE STUDY BE KEPT?

The researchers intend to keep the research data and records for approximately 5 years. Research data and records will be maintained in a de-identified state electronically on a secure network with password protection.

Any future use of this research data is required to undergo review by a Research Ethics Board.

WHOM MAY I CONTACT IF I HAVE QUESTIONS ABOUT THIS STUDY?

The Research Team:

You may contact Dr. Kirsten Fiest at 403-944-0747 with any questions or concerns about the research or your participation in this study.

Conjoint Health Research Ethics Board (CHREB):

If you have any questions concerning your rights as a possible participant in this research, please contact the Chair, Conjoint Health Research Ethics Board, University of Calgary at 403-220-7990.

AGREEMENT TO PARTICIPATE

Your decision to complete this survey will be interpreted as an indication of your agreement to participate. In no way does this waive your legal rights nor release the investigators or involved institutions from their legal and professional responsibilities.

You are free to withdraw from the study at any time.

III: Instructions

INSTRUCTIONS

The goal of this work is to generate evidence-informed consensus statements on antipsychotic prescribing practices, and facilitators and barriers to antipsychotic medication prescribing and deprescribing in patients who are experiencing critical illness or have transitioned to the hospital ward following critical illness.

This survey is **Round 1** of a multi-part consensus process. Our team conducted a systematic review and semi-structured interviews which informed statements about antipsychotic medication prescribing and deprescribing. We organized these statements into three categories: 1) perspectives of antipsychotic use 2) triggers for antipsychotic use; and 3) antipsychotic minimization and deprescribing activities. Each category includes related themes, which are itemized on the next page. You will rate (based on perceived importance) each statement on a 9-point Likert Scale. At the end of each section, you will be presented with a free-text box to suggest any experiences or practices that you think are missing.

In this round, we ask that you:

- 1. Review**

Please review each statement provided.

- 2. Rate**

Rate each statement based on your perceptions of antipsychotic use and prescribing practices in critically ill patients and patients following critical illness. Please use the full range of the 9-point scale.

- 3. Advise**

Please provide any additional experiences or practices that you think are missing from each category.

There are a total of 62 statements to review. Statements that do not reach consensus in Round 1 will be re-rated in Round 2 of the consensus process. Participant-suggested statements will also be included for rating in Round 2.

We anticipate that this round will take approximately 20 minutes to complete. You can save your responses and return to the survey any time before February 4, 2022

IV: Table of Contents

1. Perceptions of Antipsychotics
Theme 1: Perceptions of antipsychotic use for the delivery of patient care and patient/staff safety
Theme 2: Perceptions of the knowledge and frequency of antipsychotic use
Theme 3: Perception of antipsychotic guidelines and use of antipsychotics in the ICU and on the ward
2. Triggers for Antipsychotic Use
Theme 4: Clinical indications for antipsychotic use
Theme 5: Influences on decision-making for antipsychotic use, prescribing and deprescribing practices
3. Antipsychotic Minimization and Deprescribing Activities
Theme 6: Current practices for antipsychotic minimization and deprescribing
Theme 7: Deprescribing tools and strategies
4. Demographics

VI: Likert Scales

Part 1: Perceptions of Antipsychotics

This section will ask you to reflect on your current perceptions of antipsychotics, including your beliefs about the consequences of antipsychotics and their use on the ICU and in the ward.

Rate each statement based on how accurately it reflects your perceptions of antipsychotics using the scale provided. Please use the full range of the 9-point scale to rate statements from “strongly disagree” to “strongly agree.”

Theme 1: Perceptions of antipsychotic use for the delivery of patient care and patient/staff safety

1. Antipsychotic use improves patient safety (e.g., consider adverse events such as pulling lines, tubes and drains, falling out of bed, or patients hitting themselves).
2. Antipsychotic use improves staff safety (e.g., reduces physical harm to nurses or doctors).
3. Patient compliance with daily care is safer or easier when chemical restraints, such as antipsychotics, are used.
4. Antipsychotics improve patient sleep.
5. When antipsychotic medications are **avoided** in patients with delirium or agitation, there are delays in therapy (e.g., mobilization, diagnostic tests, etc.).
6. When antipsychotic medications are **used**, there are delays in therapy (e.g., neurological exams) and participation in care.
7. When antipsychotic medications are avoided, there is an increase in symptoms of family distress.
8. The use of antipsychotics provides comfort or decreases stress in the care team (i.e., by calming the patient down), irrespective of whether the underlying cause of delirium is treated.

Theme 2: Perceptions of the knowledge and frequency of antipsychotic use

1. Antipsychotics are only used for severe and significant agitation or aggression that is putting either the patient or others at risk.
2. Antipsychotics are **not** helpful for agitation.

3. Antipsychotics are prescribed more frequently when there are resource shortages (e.g., number of physical restraints available, staff available for patient monitoring), high patient volume, and high work demands.
4. Long-standing practices influence the decision to prescribe an antipsychotic (i.e., prescribing an antipsychotic has been done for the past 15-20 years, creating an “institutional inertia”).
5. Antipsychotics do not treat delirium, but rather shift patients from a state of hyperactive delirium to hypoactive delirium.
6. Staff feel confident and empowered to deprescribe antipsychotic medications.

Theme 3: Perception of antipsychotic guidelines and use of antipsychotics in the ICU and on the ward

1. Antipsychotic prescribing practices are inconsistent with current professional society guidelines on indications for antipsychotic medication use.
2. Typically, antipsychotics are used more in the ICU than on the ward.
3. The type of antipsychotic prescribed (i.e., typical vs. atypical) differs depending on the culture of the unit.
4. Culture within the ICU and ward (e.g., ideally all patients are calm and sleeping at night) contributes to antipsychotic prescribing practices.
5. Antipsychotics are preferred in comparison to continuous sedation because they have safer sedation effects.
6. Antipsychotic medications should be considered for treating delirium compared to alternative pharmacological therapies for delirium, such as benzodiazepines.
7. The prescribing and use of antipsychotics differs between day and night shifts.
8. Antipsychotic prescriptions are generally continued, despite lack of clinical indication for their ongoing appropriate use.
9. The short-term benefits of the effects of antipsychotics are often the focus for their use or are considered of higher importance than potential long-term consequences.

Are there perceptions of antipsychotics that are missing and should be included? Please use the space below to share these with us.

Part 2: Triggers for Antipsychotic Use

This section will ask you to reflect on **triggers for antipsychotic use**. This includes the main reasons for prescribing and administering antipsychotics (e.g., delirium management) and/or the continuation of use of antipsychotics in both the ICU and the ward. Rate each statement using the scale provided. Please use the full range of the 9-point scale to rate statements from “strongly disagree” to “strongly agree.”

Theme 4: Clinical indications for antipsychotic use

1. Antipsychotics should be used for hyperactive delirium (i.e., agitated delirium) treatment and management.
2. Antipsychotics should be used for hypoactive delirium treatment and management.
3. Antipsychotics should be used when non-pharmacological interventions for delirium are ineffective.
4. Antipsychotics should be used when patient, family and/or staff safety (e.g., pulling tubes, falling out of bed, physical aggression, etc.) is at risk.

5. Antipsychotics are the “path of least resistance” when dealing with patients who are agitated or experiencing hyperactive delirium, compared to physical restraints.
6. Antipsychotics help to re-establish day and night routines or mitigate sleep disturbances.
7. Environmental stressors (i.e., lack of windows, frequent noise, lights on during the night, patient isolation, and intrusive treatment) promote increased prescribing of antipsychotics.
8. Antipsychotics are useful when weaning agitated patients off of sedation.
9. Antipsychotics are useful for the management of alcohol withdrawal.
10. Antipsychotics are useful to help achieve patient sedation.
11. Antipsychotics are useful for managing symptoms of patient anxiety and panic.
12. Antipsychotics are often prescribed for their side effects (e.g., sleep) rather than their main effect.

Theme 5: Influences on decision-making for antipsychotic use, prescribing and deprescribing practices

1. The decision to prescribe an antipsychotic depends on team opinions regarding antipsychotic use during rounds.
2. There is **not** a clear understanding of clinical practice guidelines for antipsychotic medication use in the ICU and on the ward.
3. Antipsychotics are prescribed when staff advocates for antipsychotics to make care for the patient easier.
4. Antipsychotics are prescribed when necessary care for the patient and treatment are being impacted (i.e., due to agitation, delirium, etc.).
5. Staff who evaluate a patient’s records are missing information or do not have the history on the patient and why the antipsychotic was prescribed. Without this history, staff assume that the antipsychotic is necessary rather than weaning the patient off the medication.
6. Healthcare utilization costs (e.g., length of stay) plays an important role when deciding to prescribe an antipsychotic.
7. When a patient is transferred from the ICU, insufficient information about the use of antipsychotics in the ICU generates uncertainty about the continuation of antipsychotics and so patients often remain on antipsychotics due to this missing information.

Are there triggers for antipsychotic use that are missing and should be included? Please use the space below to share these with us.

Part 3: Antipsychotic Minimization and Deprescribing Activities

This section will ask you to reflect on **antipsychotic minimization and deprescribing activities** in both the ICU and on the ward. This includes rating current practices and tools used for deprescribing. Rate each statement using the scale provided. Please use the full range of the 9-point scale to rate statements from “strongly disagree” to “strongly agree.”

Theme 6: Current practices for antipsychotic minimization and deprescribing

1. Weekend discharges impact the ability to effectively deprescribe antipsychotics.
2. Antipsychotic prescribing occurs most often during night shifts.
3. Antipsychotic deprescribing frequently occurs during transitions of care (i.e., ICU to ward, ICU to home, ward to home).

4. Ongoing assessment of the patient and communication between staff about the effectiveness of the treatment (including qualitative feedback) helps to minimize antipsychotic use and promote deprescribing.
5. There is a lack of decision-making support tools or policies to guide antipsychotic deprescribing practices.
6. There is insufficient communication at transitions of care regarding current medications and deprescribing.
7. Family presence and engagement facilitates antipsychotic minimization or deprescribing of antipsychotics.
8. Non-pharmacological interventions assist in antipsychotic minimization.
9. Non-pharmacological interventions as a strategy for antipsychotic minimization are not a priority compared to other focuses (i.e., other aspects of patient care and treatment).
10. Non-pharmacological intervention experts (e.g., geriatricians) help to facilitate deprescribing of antipsychotics.
11. Deprescribing antipsychotics is **not** feasible at transitions of care (from ICU to ward) when the patient is still delirious.

Theme 7: Deprescribing tools and strategies

1. There is a need for a direct and efficient communication tool within transfer or discharge summaries between prescribers at transitions of care to identify continued medications such as antipsychotics and to provide discontinuation recommendations.
2. There is a need for additional antipsychotic medication prescribing accountability to facilitate deprescribing (e.g., automatic stop dates, no “as needed” dosing allowed, force function alerts, flags for review, and reassessment dates).
3. Additional medication reconciliation should occur at transitions of care to identify antipsychotics that have been continued without clear ongoing clinical indication.
4. Formal education sessions on indications for antipsychotic medication prescribing and deprescribing are needed.
5. There is a need for expert consultations on medication management upon transitions of care (e.g., geriatrics consultation, outpatient follow-up).
6. There is a need for the creation of pharmacist-driven deprescribing strategies or algorithms.
7. There is a need for tapering protocols and discharge medication care bundles.
8. There is a need for policy development on antipsychotic prescribing practices.
9. There should be practice audits for feedback to prescribers on antipsychotic prescribing practices with non-punitive mechanisms.

Are there current practices or strategies for antipsychotic minimization and deprescribing that are missing and should be included? Please use the space below to share these with us.

V: Demographics

Demographic Questions

We are collecting personal demographic information to describe our participants in aggregate. Please note that your demographic information will be stored anonymously in a password protected database that is only accessible to the study research team. If you are not

comfortable answering any of the below questions you are welcome to skip any or all of those you do not wish to answer.

11. What is your age group?

- ☐ <20 years
- ☐ 20-29 years
- ☐ 30-39 years
- ☐ 40-49 years
- ☐ 50-59 years
- ☐ ≥60 years

12. What is the sex you were assigned at birth?

- ☐ Male
- ☐ Female
- ☐ Prefer not to answer

13. What is your gender identity?

- ☐ Man
- ☐ Woman
- ☐ Non-binary / third gender
- ☐ Two-Spirit (*Two-Spirit is a cultural term used by some Indigenous people to mean a person who has both a male and female spirit*)
- ☐ Prefer to self-describe: _____
- ☐ Prefer not to answer

14. Please indicate your ethnic or cultural group (select all that apply)

Please note that the examples provided are non-exhaustive and are meant to be a guide to help you respond to the question.

- ☐ First Nations
- ☐ Inuit
- ☐ Métis
- ☐ Other North American Origins (e.g., Canadian, American, Acadian)
- ☐ British Isles Origins (e.g., English, Irish, Scottish)
- ☐ Western European Origins (e.g., French, German, Dutch)
- ☐ Northern European Origins (e.g., Swedish, Finnish, Icelandic)
- ☐ Eastern European Origins (e.g., Russian, Latvian, Hungarian)
- ☐ Southern European Origins (e.g., Albanian, Italian, Spanish)
- ☐ Caribbean Origins (e.g., Cuban, Dominican, Bahamian)
- ☐ Latin, Central and South American Origins (e.g., Brazilian, Mexican, Venezuelan)
- ☐ Central and West African Origins (e.g., Cameroonian, Nigerian, Sierra Leonean)
- ☐ North African Origins (e.g., Egyptian, Moroccan, Sudanese)
- ☐ South and East African Origins (e.g., Ethiopian, Rwandan, Zimbabwean)
- ☐ West Central Asian and Middle Eastern Origins (e.g., Afghan, Iranian, Palestinian)
- ☐ South Asian Origins (e.g., Bangladeshi, Pakistani, Punjabi)
- ☐ East and Southeast Asian Origins (e.g., Chinese, Japanese, Vietnamese)
- ☐ Ocean and Pacific Islands Origins (e.g., Australian, Fijian, Polynesian)
- ☐ Prefer not to answer
- ☐ Other, please specify: _____

15. What is your place of residence where you are currently working?

- ☐ Alberta
- ☐ British Columbia
- ☐ Manitoba
- ☐ New Brunswick
- ☐ Newfoundland and Labrador
- ☐ Northwest Territories
- ☐ Nova Scotia
- ☐ Nunavut
- ☐ Ontario
- ☐ Prince Edward Island
- ☐ Quebec
- ☐ Saskatchewan
- ☐ Yukon

16. What is your current role?

- ☐ Licensed practical nurse
- ☐ Registered nurse
- ☐ Nurse practitioner
- ☐ Resident
- ☐ Fellow
- ☐ Attending physician
- ☐ Pharmacist
- ☐ Other (please specify): _____

17. [If applicable] What physician role do you identify as?

- ☐ Primary clinician
- ☐ Clinician scientist
- ☐ Clinician educator
- ☐ Clinician administrator
- ☐ Other (please specify): _____

18. How many years have you worked in your current role?

- ☐ Please specify: _____

19. How many years have you worked in critical care or within the hospital environment?

- ☐ Please specify: _____

20. What type of institution are you currently working in?

- ☐ Academic
- ☐ Non-academic
- ☐ Regional
- ☐ Urban
- ☐ Other (please specify): _____

21. How many beds in total does your hospital have?

- ☐ ≤250
- ☐ 251-499
- ☐ 500-1000
- ☐ >1000

☐ Other (please specify): _____

VII: Closing Message

Thank you for participating in the survey, we highly value your time and insight. Your response has now been recorded. You will receive a summary of the results by email in the coming weeks.

If you have any questions about this survey please contact the study coordinator via email at njaworsk@ucalgary.ca. All information will be kept strictly confidential. Your decision to participate will not impact your employment now or at any time in the future.

Appendix 4.3 Antipsychotic Delphi Round 2 Questionnaire: Likert Scale Rating of Consensus Statements

I. Introduction (email)

Dear colleagues,

Thank you for agreeing to participate in the Delphi consensus process on antipsychotic prescribing and administration practices in current and former critically ill patients. The aim of this work is to generate national evidence-informed consensus statements on antipsychotic prescribing practices, minimization, and deprescribing activities.

This survey is **Round 2** of a multi-part consensus process. We expect this round to take approximately 10 minutes to complete. You can save your responses and return to the survey at any time before **March 21, 2022 at 11:59 pm MST**.

This survey contains the list of statements that did not reach consensus in Round 1, and additional items suggested by participants. Your information will be held in strict confidence and will not be associated with any individual answer.

Follow this link to the Survey:

Or copy and paste the URL below into your internet browser:

Thank you again for your time and participation. Please email our team directly if you have any questions.

Sincerely, Natalia Jaworska & Kirsten Fiest

II. Implied Consent



UNIVERSITY OF CALGARY IMPLIED CONSENT TO PARTICIPATE IN RESEARCH

TITLE: Facilitators and barriers to deprescribing antipsychotic medications in critically ill adult patients at transitions of care: A mixed methods study

SPONSOR: None.

FUNDER: This study is unfunded.

INVESTIGATORS: Dr. Natalia Jaworska, Dr. Kirsten M. Fiest

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This consent form is only part of the process of informed consent. It should give you the basic idea of what the research is about and what your participation will involve. If you would like more detail about something mentioned here, or information not included here, please ask. Take the time to read this carefully and to understand any accompanying information.

You were identified as a possible participant in this study because you are a hospital ward or critical care physician, nurse, or pharmacist who works with either critically ill patients or those following critical illness who receive antipsychotic medications. Your participation in this research study is voluntary.

Antipsychotic medications are commonly prescribed for critically ill patients. Up to 42% of patients receive an antipsychotic in the intensive care unit (ICU). These antipsychotic medications are prescribed for various reasons but are typically prescribed for the symptoms of delirium. Randomized studies show antipsychotics do not alter the course of delirium. Long-term use is associated with increased sudden death, falls, and cognitive impairment. Still, one third of patients prescribed antipsychotics in the ICU will go home with an ongoing prescription without a clinical indication. Limited literature is available to understand the factors, facilitators, and barriers that influence antipsychotic prescribing and deprescribing practices in patients following critical illness.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to understand the factors that influence antipsychotic medication prescribing and administration practices of critical care and ward healthcare providers (physicians, nurses, and pharmacists) in patients with or following critical illness, and to identify facilitators and barriers to deprescribing antipsychotic medication in adult patients following critical illness in the ICU and during hospitalization. The goal of the survey is to gain consensus on healthcare provider experiences and identified facilitators and barriers to antipsychotic deprescribing through repeated rounds of surveys.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 20 to 30 people will take part in this study Canada wide. Approximately 10 people will take part in this study through the University of Calgary.

WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY?

If you volunteer to participate in this study, the researcher will ask you to do the following:

Complete multiple rounds of surveys (expect two to three), rating from 1 to 9, experiences related to antipsychotic prescribing practices as well as facilitators and barriers to antipsychotic medication deprescribing for critically ill patients and those patients who have moved from the ICU to the hospital ward.

Each round of surveys should take no more than 20 minutes to complete.

Surveys will occur approximately every 3 weeks during which you will have 2 weeks to complete the survey.

ARE THERE ANY POTENTIAL RISKS OR DISCOMFORTS THAT I CAN EXPECT FROM THIS STUDY?

There are no risks associated with your participation.

HOW LONG WILL I BE IN THIS STUDY?

You will be in this study for approximately 6 to 9 weeks during which you will be asked to complete and anticipated 2 to 3 surveys in at approximately 3-week intervals. You may be asked to extend your time in the study or complete additional rounds of surveys if consensus cannot be achieved on items with the previously completed surveys.

ARE THERE ANY POTENTIAL BENEFITS IF I PARTICIPATE?

If you agree to take part in this study, there may or may not be a direct benefit to you. By choosing to take part, you will have the opportunity to provide data to develop an understanding of antipsychotic medication prescribing practices for patients with or following critical illness.

CAN I STOP BEING IN THE STUDY?

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Use of the data collected may include academic presentations or papers.

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Any future use of this research data is required to undergo review by a Research Ethics Board.

WHOM MAY I CONTACT IF I HAVE QUESTIONS ABOUT THIS STUDY?

The Research Team:

You may contact Dr. Kirsten Fiest at 403-944-0747 with any questions or concerns about the research or your participation in this study.

Conjoint Health Research Ethics Board (CHREB):

If you have any questions concerning your rights as a possible participant in this research, please contact the Chair, Conjoint Health Research Ethics Board, University of Calgary at 403-220-7990.

AGREEMENT TO PARTICIPATE

Your decision to complete this survey will be interpreted as an indication of your agreement to participate. In no way does this waive your legal rights nor release the investigators or involved institutions from their legal and professional responsibilities.

You are free to withdraw from the study at any time.

III. Instructions

Thank you for participating in Round 1 of the Delphi consensus survey on antipsychotic prescribing and deprescribing practices in current or former critically ill patients.

This survey is **Round 2** of a multi-part consensus process. This survey contains the initial list of statements that did not reach consensus in Round 1, and additional items suggested by participants. This survey contains 33 statements for consideration.

The goal of this work is to generate evidence-informed consensus statements on antipsychotic prescribing practices, and identify priority facilitators and barriers to antipsychotic medication prescribing and deprescribing in patients who are experiencing or have experienced critical illness. For this round, we ask that you provide a score on the 9-point Likert scale indicating whether you strongly disagree (1) or strongly agree (9) with the statement. **To help achieve consensus, please consider selecting a response closer to either end of the scale to indicate your opinion of the statement.**

We expect this survey to take approximately 10 minutes to complete. The survey will close on **March 21, 2022 at 11:59 pm MST**. You may save your responses and return to the survey at any time. Please contact our team if you have any questions.

IV. Table of Contents

5. Perceptions of Antipsychotics
 - Theme 1:** Perceptions of antipsychotic use for the delivery of patient care and patient/staff safety
 - Theme 2:** Perceptions of the knowledge and frequency of antipsychotic use
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7. Antipsychotic Minimization and Deprescribing Activities
 - Theme 6:** Current practices for antipsychotic minimization and deprescribing
 - Theme 7:** Deprescribing tools and strategies

V. Likert Scales

Part 1: Perceptions of Antipsychotics

This section will ask you to reflect on your current perceptions of antipsychotic medication use, including your beliefs about the consequences of antipsychotics and their use in the ICU and on the hospital ward. Rate each statement based on how accurately it reflects your perceptions of antipsychotics using the scale provided. Please rate statements from “strongly disagree” to “strongly agree.”

Theme 1: Perceptions of antipsychotic use for the delivery of patient care and patient/staff safety

1. Antipsychotic use improves patient safety (e.g., consider adverse events such as pulling lines, tubes and drains, falling out of bed, or patients hitting themselves).

2. Antipsychotic use improves staff safety (e.g., reduces physical harm to nurses or doctors).
3. Patient compliance with daily care is safer or easier when chemical restraints, such as antipsychotics, are used.
4. Antipsychotics are commonly used for sleep.
5. When antipsychotic medications are avoided in patients with delirium or agitation, there are delays in therapy (e.g., mobilization, diagnostic tests, etc.).
6. When antipsychotic medications are used in patients with delirium or agitation, there are delays in therapy (e.g., neurological exams) and participation in care.
7. When antipsychotic medications are avoided, there is an increase in families experiencing symptoms of distress.
8. The use of antipsychotics provides comfort or decreases stress in the care team (i.e., by calming the patient down), irrespective of whether the underlying cause of delirium is treated.

Added Items to Theme 1:

9. Chemical restraints, such as antipsychotics, are a gentler form of restraint and are better tolerated by patients, as opposed to physical restraints.
10. Staff may be reluctant to administer antipsychotics due to lack of knowledge regarding the value of antipsychotics.

Theme 2: Perceptions of the knowledge and frequency of antipsychotic use

1. Antipsychotics are only used for severe and significant agitation or aggression that is putting either the patient or others at risk.
2. Antipsychotics are prescribed more frequently when there are resource shortages (e.g., number of physical restraints available, staff available for patient monitoring), high patient volume, and high work demands.
3. Staff feel confident and empowered to deprescribe antipsychotic medications.

Theme 3: Perception of antipsychotic guidelines and use of antipsychotics in the ICU and on the ward

1. Antipsychotic prescribing practices are inconsistent with current professional society guidelines on indications for antipsychotic medication use.
2. Antipsychotics are preferred in comparison to continuous sedation because they have safer sedation effects.
3. The prescribing and use of antipsychotics differs between day and night shifts.
4. Antipsychotic prescriptions are generally continued, despite lack of clinical indication for their ongoing appropriate use.

Added items to theme 3:

5. There is a pervasive perception amongst staff that the use of antipsychotics for treating delirium is guided by strong evidence.
6. The risk-benefit ratio of antipsychotic prescribing and use is rarely discussed with the substitute decision maker for informed consent.
7. Current professional society guidelines outlining recommendations on when antipsychotic medication should or should not be used are not generally agreed upon amongst staff.
8. Current professional society guidelines on antipsychotic medication use do not provide the quality and quantity of evidence used to support the guidelines.

9. Other ICU care team members put pressure on the attending physician to prescribe antipsychotics, which influences prescribing practices.

Part 2: Triggers for Antipsychotic Use

This section will ask you to reflect on **triggers for antipsychotic use**. This includes the main reasons for prescribing and administering antipsychotics (e.g., delirium management) and/or the continuation of use of antipsychotics in both the ICU and the ward. Rate each statement using the scale provided. Please rate statements from “strongly disagree” to “strongly agree.”

Theme 4: Clinical indications for antipsychotic use

1. Antipsychotics help to re-establish day and night routines or mitigate sleep disturbances.
2. Antipsychotics are useful when weaning agitated patients off continuous sedation to facilitate extubation.
3. Antipsychotics are useful to help achieve patient sedation.
4. Antipsychotics are useful for managing symptoms of patient anxiety and panic.

Added items to theme 4

5. Antipsychotics are safe for all ICU patients.
6. Antipsychotic medications are used to avoid the use of continuous IV sedative infusions with hyperactive delirium or agitation.
7. Antipsychotics are used to manage the symptoms of agitation or hyperactive delirium when there is an inability to modify certain underlying medical drivers responsible for patient symptoms.

Theme 5: Influences on decision-making for antipsychotic use, prescribing and deprescribing practices

1. Staff who evaluate a patient's records **may be** missing information, do not have the history on the patient, or the confidence (e.g., junior staff) to question why the antipsychotic was prescribed. Therefore, staff assume that the antipsychotic is necessary rather than weaning the patient off the medication.

Part 3: Antipsychotic Minimization and Deprescribing Activities

This section will ask you to reflect on **antipsychotic minimization and deprescribing activities** in both the ICU and on the ward. This includes rating current practices and tools used for deprescribing. Rate each statement using the scale provided. Please rate statements from “strongly disagree” to “strongly agree.”

Theme 6: Current practices for antipsychotic minimization and deprescribing

1. Weekend discharges impact the ability to effectively deprescribe antipsychotics.
2. Antipsychotic prescribing occurs most often during night shifts.
3. Antipsychotic deprescribing frequently occurs during transitions of care (i.e., ICU to ward, ICU to home, ward to home).
4. Deprescribing antipsychotics is not feasible at transitions of care (from ICU to ward) when the patient is still delirious.

Theme 7: Deprescribing tools and strategies

Added items to theme 7:

1. There is a need for an informed consent process and documentation for antipsychotic use and administration.

Appendix 4.4 Antipsychotic Delphi Round 3 Questionnaire: Weighted Rankings of Consensus Statements

I. Instructions

Thank you for participating in Round 2 of the Delphi consensus survey on antipsychotic prescribing and deprescribing practices in current or former critically ill patients.

This survey is **Round 3** (of 3) of a multi-part consensus process. This survey contains all the items that reached consensus in both Round 1 and Round 2. For this round, we ask that you provide a weighed ranking of the items that reached consensus. Please allocate a value to each item based on the perceived understanding of antipsychotic use in critically ill patients and/or your perceived importance of antipsychotic minimization and deprescribing activities. Allocated values may range from **0 (low importance) to 100 (high importance)**, however, the overall total allocated value for each theme **must total to 100 points**. You will receive an error message if your score does not total to 100 points. **We suggest that you read all items first before assigning a value to each item.**

For example, if you wanted to allocate equal importance across 5 items, a value of 20 would be allocated to each item. Alternatively, the values could be dispersed to indicate greater variability in the importance of the item. Scores of 0 are allowable.

Please note: a lower ranking does not mean that the item will be excluded from future policy considerations, just considered lower priority.

We expect this survey to take approximately 20 minutes to complete. The survey will close on **April 25th at 11:59 pm MST**. You may save your responses and return to the survey at anytime. Please contact our team if you have any questions.

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 - Theme 6:** Current practices for antipsychotic minimization and deprescribing
 - Theme 7:** Deprescribing tools and strategies

Please note: Themes 1-3 (Perceptions of Antipsychotics) will not receive a priority ranking as these are subjective to individual experiences. The results from Round 1 and 2 will be presented in the manuscript as consensus or non-consensus items only.

Triggers for Antipsychotic Use

This section will ask you to reflect on **triggers for antipsychotic use**. This includes the main reasons for prescribing and administering antipsychotics (e.g., delirium management) and/or the continuation of use of antipsychotics in both the ICU and the ward. Please rate each item by assigning a weight value between 0-100 based on the most common triggers for antipsychotic use. For example, if an item frequently occurred, or you think the item has a significant impact, you should rank this as a higher score. If the items are of equal significance, you may rank them the same (e.g., 12.5-12.5-12.5-12.5-12.5-12.5-12.5-12.5). Scores of 0 are allowable.

Note: Allocated values may range from 0-100 but the overall total summed value must equal 100 points.

Theme 4: Clinical indications for antipsychotic use

1. Antipsychotics should be used for hyperactive delirium (i.e., agitated delirium) treatment and management.
2. Antipsychotics should be used when non-pharmacological interventions for delirium are ineffective.
3. Antipsychotics should be used when patient, family and/or staff safety (e.g., pulling tubes, falling out of bed, physical aggression, etc.) is at risk.
4. Environmental stressors (i.e., lack of windows, frequent noise, lights on during the night, patient isolation, and intrusive treatment) promote increased prescribing of antipsychotics.
5. Antipsychotics are often prescribed for their side effects (e.g., sleep) rather than their main effect.
6. Antipsychotic medications are used to avoid the use of continuous IV sedative infusions with hyperactive delirium or agitation.
7. Antipsychotics are used to manage the symptoms of agitation or hyperactive delirium when there is an inability to modify certain underlying medical drivers responsible for patient illness (e.g., exposure to medically necessary medications that increase the risk of delirium).

Theme 5: Influences on decision-making for antipsychotic use, prescribing and deprescribing practices

1. The decision to prescribe an antipsychotic depends on team opinions regarding antipsychotic use during rounds.
2. There is not a clear understanding of clinical practice guidelines for antipsychotic medication use in the ICU and on the ward.
3. Antipsychotics are prescribed when staff advocates for antipsychotics to make care for the patient easier.
4. Antipsychotics are prescribed when necessary care for the patient and treatment are being impacted (i.e., due to agitation, delirium, etc.).
5. When a patient is transferred from the ICU, insufficient information about the use of antipsychotics in the ICU generates uncertainty about the continuation of antipsychotics and so patients often remain on antipsychotics due to this missing information.
6. Staff who evaluate a patient's records may be missing information, do not have the history on the patient, or the confidence (e.g., junior staff) to question why the antipsychotic was prescribed. Therefore, staff assume that the antipsychotic is necessary rather than weaning the patient off the medication.

Antipsychotic Minimization and Deprescribing Activities

This section will ask you to reflect on **antipsychotic minimization and deprescribing activities** in both the ICU and on the ward. This includes rating current practices and tools used for deprescribing. Rate each statement using the scale provided. Please rate each item by assigning a weight value between 0-100 based on the most importance antipsychotic minimization and deprescribing activities. For example, if an activity frequently occurred, or you

think the item has a significant impact, you should rank this as a higher score. If the items are of equal significance, you may rank them the same (e.g., 14.2-14.3-14.3-14.3-14.3-14.3-14.3). Scores of 0 are allowable.

Note: Allocated values may range from 0-100 but the overall total summed value must equal 100 points.

Theme 6: Current practices for antipsychotic minimization and deprescribing

1. Ongoing assessment of the patient and communication between staff about the effectiveness of the treatment (including qualitative feedback) helps to minimize antipsychotic use and promote deprescribing
2. There is a lack of decision-making support tools or policies to guide antipsychotic deprescribing practices.
3. There is insufficient communication at transitions of care regarding current medications and deprescribing.
4. Family presence and engagement facilitates antipsychotic minimization or deprescribing of antipsychotics.
5. Non-pharmacological interventions assist in antipsychotic minimization.
6. Non-pharmacological interventions as a strategy for antipsychotic minimization are not a priority compared to other focuses (i.e., other aspects of patient care and treatment).
7. Non-pharmacological intervention experts (e.g., geriatricians) help to facilitate deprescribing of antipsychotics.

Theme 7: Deprescribing tools and strategies

1. There is a need for a direct and efficient communication tool within transfer or discharge summaries between prescribers at transitions of care to identify continued medications such as antipsychotics and to provide discontinuation recommendations.
2. There is a need for additional antipsychotic medication prescribing accountability to facilitate deprescribing (e.g., automatic stop dates, no “as needed” dosing allowed, force function alerts, flags for review, and reassessment dates).
3. Additional medication reconciliation should occur at transitions of care to identify antipsychotics that have been continued without clear ongoing clinical indication.
4. Formal education sessions on indications for antipsychotic medication prescribing and deprescribing are needed.
5. There is a need for expert consultations on medication management upon transitions of care (e.g., geriatrics consultation, outpatient follow-up).
6. There is a need for the creation of pharmacist-driven deprescribing strategies or algorithms.
7. There is a need for tapering protocols and discharge medication care bundles.
8. There is a need for policy development on antipsychotic prescribing practices.
9. There should be practice audits for feedback to prescribers on antipsychotic prescribing practices with non-punitive mechanisms.

CHAPTER 5: DISCUSSION

5.1 Summary of Main Findings

This thesis presents three papers that addresses knowledge gaps related to facilitators and barriers to antipsychotic prescribing practices in adult patients with and following critical illness using multiple methodologies and data sources to define priority statements related to antipsychotic prescribing minimization and deprescribing activities. Paper 1 described the perspectives of healthcare professionals – physicians, nurses, and pharmacists – on antipsychotic prescribing practices for patients with and following critical illness, Paper 2 mapped the perceptions and practices of antipsychotic prescribing of healthcare professionals in acute care settings and catalogued in-hospital deprescribing strategies, and Paper 3 synthesized priority statements by consensus on antipsychotic minimization strategies and antipsychotic deprescribing activities for adult patients with and following critical illness.

The objective of Paper 1 was to identify and describe relevant domains and constructs from the TDF that influenced antipsychotic medication prescribing and deprescribing practices among physicians, nurses, and pharmacists that care for critically ill adult patients during and following critical illness. Semi-structured interviews were conducted with twenty-one critical care and ward healthcare professionals including 11 physicians, five nurses, and five pharmacists. Using deductive thematic analysis following the TDF to identify and describe constructs within relevant domains, seven TDF domains were identified as relevant from the analysis:

Social/professional role & identity; Beliefs about capabilities; Reinforcement; Motivations & goals; Memory, attention & decision processes; Environmental context & resources; and Beliefs about consequences. Participants reported antipsychotic prescribing for multiple indications beyond delirium and agitation including patient and staff safety, sleep management, and to address environmental stressors such as staff availability and workload. Participants additionally identified potential antipsychotic deprescribing strategies to reduce ongoing antipsychotic medication prescriptions for critically ill patients including direct communication tools between

prescribers at transitions of care, and antipsychotic medication prescribing accountability strategies (e.g., automatic stop dates, no as needed dosing). This qualitative study reported on several factors influencing established antipsychotic medication prescribing and deprescribing practices. The results from this study suggest that the primary factors limiting adherence to current antipsychotic prescribing guideline recommendations were the prescription of antipsychotics to maintain patient and staff safety to facilitate providing care to patients with hyperactive delirium and agitation.

Paper 2 characterized antipsychotic medication prescribing and deprescribing practices, described healthcare professional perceptions on antipsychotic prescribing and deprescribing practices, and reported on antipsychotic deprescribing strategies within acute care. A scoping review of five databases identified 4528 studies that were screened with 80 studies included – 49 of which evaluated ICU antipsychotic prescribing practices and the remaining 31 which evaluated inpatient and emergency department antipsychotic prescribing practices. Healthcare professionals across all acute care settings (intensive care, inpatient, emergency department) perceived that haloperidol was prescribed most frequently, while when measured in observational cohort studies quetiapine prescribing was more common. Indications for antipsychotic prescribing were delirium and agitation across all acute care settings. Quetiapine was the most frequently prescribed antipsychotic on an ongoing basis at hospital discharge. Perspectives on antipsychotic prescribing practices among healthcare professionals mapped to the TDF identified four domains important for influencing healthcare professional prescribing practices: *Knowledge* (e.g., knowledge of conditions requiring antipsychotics), *Beliefs about capabilities* (e.g., perceived competence regarding antipsychotic prescribing contexts such as delirium), *Beliefs about consequences* (e.g., beliefs surrounding antipsychotic efficacy for delirium), and *Environmental context and resources* (e.g., available screening tools and protocols to guide antipsychotic prescribing). Three studies reported in-hospital antipsychotic deprescribing strategies within the ICU environment focused on pharmacist-driven

deprescribing authority, handoff tools, and educational sessions. This scoping review and narrative synthesis highlighted the differences between what healthcare professional perceptions and true prescribing practices are, with few in-hospital deprescribing strategies described. These results suggested that antipsychotic minimization and deprescribing strategies require an approach that targets both individual prescribing and deprescribing practice beliefs and current established health system processes to develop sustainable reductions in antipsychotic prescribing.

In bringing the results together from both Paper 1 and Paper 2, Paper 3 identified evidence-informed consensus statements for antipsychotic minimization activities and antipsychotic deprescribing strategies for patients with and following critical illness to support best clinical prescribing practices. In this nationwide modified Delphi consensus process, stakeholders completed three rounds of virtual polling of statements to rate and subsequently rank identified statements informed by semi-structured interviews and the scoping review (Paper 1 and 2) in three domains: perceptions on antipsychotic medication use, triggers for antipsychotic prescription, and antipsychotic minimization and deprescribing activities. Stakeholders perceived patient and staff safety, patient sleep, and clinician concern for team members caring for agitated patients as common indications for antipsychotic use. Prioritized statements on antipsychotic minimization and deprescribing strategies emphasized six strategies focused on limiting antipsychotic prescribing to patients (1) with hyperactive delirium, (2) at risk to themselves, their family, and/or staff due to agitation, and (3) whose care and treatment are being impacted due to agitation or delirium, and prioritizing (4) communication among staff about antipsychotic effectiveness, (5) direct and efficient communication tools on antipsychotic deprescribing at transitions of care, and (6) medication reconciliation at transitions of care. The results of this study highlighted the importance of two considerations when developing interventions for antipsychotic minimization and deprescribing: (1) defining appropriate indications for antipsychotic administration in critically ill patients, and (2)

establishing clear verbal and electronic communication mechanisms at transitions of care to address continued antipsychotic prescriptions and to provide discontinuation recommendations.

The research presented in this thesis aimed to understand the factors that contribute to antipsychotic prescribing and deprescribing practices in critically ill patients during the various phases of their hospitalization in the context of current guidelines recommending against their routine use. The overarching goal was to develop consensus statements and stakeholder recommendations for potential future implementation of clinical care pathways to minimize antipsychotic overprescribing. The three papers represent an investigation into the facilitators and barriers related to structure, process, and outcome measures contributing to antipsychotic prescribing practices for critically ill patients, an evaluation of the literature on current antipsychotic prescribing practices by indication, medication preferences, and healthcare professional prescribing perceptions, and a catalogue of stakeholder informed consensus statements on antipsychotic minimization and deprescribing strategies.

5.2 Findings in the Context of Existing Literature

Antipsychotic medication use for delirium, agitation, and sleep management for critically ill patients is well-documented within the literature and remains a pervasive clinical practice among healthcare professionals [17, 38, 62, 63]. The continuation of antipsychotic medications following ICU and hospital discharge in antipsychotic-naïve patients is common despite guideline recommendations suggesting that antipsychotic medication administration should be time-limited with the goal of discontinuation as soon as no longer necessary [20, 38, 50, 55, 64, 65]. To understand the factors informing antipsychotic prescribing practices in critically ill patients throughout their hospitalization, more knowledge regarding specific barriers and facilitators to guideline adherence related to antipsychotic prescribing practices is needed.

Barriers to the general adherence to guideline-recommended clinical practices have been previously evaluated. Lack of awareness, familiarity, agreement, self-efficacy, and outcome expectancy as well as inertia of previous practice have been identified as key drivers that limit the uptake of clinical practice guidelines [66]. However, the care of critically ill patients introduces unique challenges for guideline adherence frequently influenced by external patient-related barriers that limit the feasibility of compliance [67]. Documentation of external patient-related barriers and healthcare professional perceptions toward antipsychotic prescribing and deprescribing in critically ill patients has not previously been evaluated using a validated methodological framework. Paper 1 described several specific external barriers limiting antipsychotic deprescribing related to patient and staff safety, sleep management, and as a mechanism to manage environmental stressors such as staff availability and workload. To date, focus on antipsychotic medication prescribing practices for critically ill patients has centered on the use of antipsychotics for the prevention and management of delirium contextualized in the perception that antipsychotic use is an appropriate strategy for delirium despite evidence to the contrary [68-70].

Deprescribing aims to formalize the process of withdrawal or dose minimization of an inappropriate medication with the goal of managing polypharmacy and improving patient- and system-level outcomes [57]. Strategies to facilitate antipsychotic deprescribing within the ICU have been evaluated and are documented in Paper 2. Current evidence for antipsychotic deprescribing has focused on the use of discontinuation algorithms, hand-off tools, multidisciplinary education, and pharmacist-driven tapering schedules [59, 60, 71]. Variable efficacy in these strategies to reduce antipsychotic prescribing effectively and sustainably during hospitalization and at hospital discharge were found. Challenges with rational and effective deprescribing of potentially inappropriate medications spans hospital settings and may provide insight into the challenges experienced in achieving effective deprescribing of antipsychotics in intervention studies in the ICU setting. For example, Scott and colleagues evaluated strategies

to overcome facilitators and barriers to deprescribing potentially inappropriate medications within the hospital setting using Nominal Group Techniques with a panel of pharmacist and geriatrician experts [72]. Four intervention components were identified to support engagement with in-hospital deprescribing: (1) an organizational action plan to prioritize deprescribing; (2) training activities to address pharmacists' beliefs about negative deprescribing consequences; (3) restructuring pharmacists' working patterns to facilitate their contribution to deprescribing decisions; and (4) sharing experiences of successfully engaging patients/family in deprescribing conversations [72]. Paper 3 aimed to apply similar methodological principles to identify specific consensus statements relevant to antipsychotic prescribing and deprescribing practices in the critical care setting as a foundation to developing broad intervention components applicable to the unique and challenging ICU environment. The results from this study support previously documented principles for in-hospital deprescribing with an explicit focus on the use of bidirectional communication tools embedded in transfer and discharge summaries and additional purposeful medication reconciliation at transitions of care to facilitate antipsychotic minimization and deprescribing.

In conclusion, the findings in the three papers presented in this thesis align and build upon current literature surrounding antipsychotic prescribing and deprescribing in critically ill patients during their hospitalization. These findings expand on existing literature on antipsychotic prescribing practices in critically ill patients and generate future research questions and opportunities for implementation into multicomponent interventions. Antipsychotic medication prescribing in the ICU may at times be necessary due to the challenging clinical circumstances. Novel strategies are needed to facilitate structured antipsychotic prescribing practices that address both the prescribing and deprescribing process. The overall goal of structured antipsychotic medication prescribing and deprescribing practices in the ICU should aim to encourage utilization and optimization of evidence-based non-pharmacologic interventions for delirium and/or agitation prevention and sleep management.

5.3 Challenges and Limitations in Studying Antipsychotic Prescribing Practices in the Critically Ill

This section describes challenges and limitations in studying antipsychotic prescribing practices in the critically ill. The evaluation of antipsychotic prescribing practices in the ICU requires several additional considerations; the availability and/or feasibility of alternative non-pharmacologic and pharmacologic interventions for delirium subtypes, agitation, and sleep disturbances, healthcare resource constraints influencing prescribing practices, and newly acquired complex psychiatric complications contributing to antipsychotic prescribing practices.

5.3.1 Available Alternative Interventions for Delirium Subtypes, Agitation, and Sleep Disturbances

Healthcare professionals tasked with caring for critically ill patients often struggle to identify alternatives to antipsychotic medications to manage symptoms of agitation related to delirium or ongoing sleep disturbances if non-pharmacologic interventions do not improve a patient's clinical status. With few effective pharmacologic alternatives available for acutely agitated patients and legitimate concerns regarding patient and staff safety, patient- and clinician-related barriers in concert with ICU contextual barriers (e.g., competing priorities, cultural "inertia") are likely to lead to antipsychotic prescribing [73]. Practical problems exist in the care of critically ill patients that challenge even the most well-intentioned healthcare professionals where the risks of patient and staff safety outweigh the risks of harm from antipsychotic prescribing. Implementation of strategies that minimize antipsychotic prescribing and emphasize non-pharmacologic interventions remains complex and are likely to be

imperfect. Targeting complete elimination of antipsychotic use within the ICU is impractical and unlikely to be feasible given these clinical challenges.

5.3.2 Available Human Resources in Resource Constrained Healthcare Systems

Human resource constraints within healthcare systems and ICUs are a concern and can limit the adoption of antipsychotic minimization and deprescribing strategies due to challenges to implement more resource-intensive non-pharmacologic approaches to delirium, agitation, and sleep management. Complete delivery of non-pharmacologic care bundles such as the ABCDEF bundle in critically ill patients is associated with several favorable outcomes including a lower likelihood of mortality, delirium, and physical restraint use [19]. However, in circumstances of human resource constraint or in resource-poor countries, the delivery of all components of currently recommended non-pharmacologic care bundles may be perceived as or may truly be not possible, leading to a greater reliance on pharmacologic interventions with antipsychotic medications for delirium, agitation, and sleep management. Utilizing methodological frameworks from implementation science principles that adapt evidence-based practice to local resource constraints may help leverage available resources in innovative ways to both better implement non-pharmacologic strategies and additionally minimize pharmacologic management of delirium, agitation, and sleep [74].

5.3.3 Psychiatric Complications During and Following Critical Illness

Patients who experience critical illness face an increased risk of developing psychiatric complications as part of a clinical syndrome referred to as post-ICU syndrome (PICS) [75]. Trauma-related symptoms with and without associated moderate to severe depressive symptoms in ICU survivors have been associated with more chronic sleep disturbances [76]. Chronic sleep disturbances and mental health complications related to critical illness increases

the risk of exposure to pharmacologic interventions such as antipsychotics [77]. Fragmentation of the healthcare system and limited access to physical and psychological support for patients at high-risk of PICS following hospitalization risks creating an environment prime for the use of pharmacologic interventions such as antipsychotics to manage challenging symptoms that may be slow to improve or may not improve at all. Implementation of strategies to deprescribe antipsychotics in this complex patient population need to be flexible enough to include patient-centered collaborative considerations for individualized programs aimed at dose minimization and/or deprescribing, coupled with non-pharmacologic long-term interventions.

5.4 Clinical and Public Health Implications

Health services research is a multidisciplinary research field that aims to improve the way in which health services are either financed, organized, planned, and/or delivered through scientific investigation [78, 79]. Various methodologies help to inform clinically relevant research questions addressing healthcare access, utilization, quality, outcomes, or cost parameters [79]. Defined in its advent as a mechanism to address assessment and accountability within the healthcare system, the primary goal of health services research is to drive healthcare reform and inform managerial and policy decision-making [80, 81].

The intersection of health services research and public health builds evidence for understanding system factors driving patient- and population-level health in a way that provides health leaders and policymakers with the necessary information for evidence-based, science-driven decision-making [82]. The following three areas of clinical implications are supported by the evidence within this thesis and existing scientific literature which health leaders and policymakers may leverage when addressing the negative pharmacologic consequences related to delirium and/or agitation and antipsychotic overprescribing.

5.4.1 Causal Inferences for Antipsychotic Medication Prescribing Practices

Guidelines and a growing body of literature on the clinical inefficacy of antipsychotic prescribing for delirium and/or agitation in critically ill patients has not led to a substantial reduction in antipsychotic medication prescribing [83]. Inappropriate antipsychotic prescribing in critically ill patients has been well-documented in the literature [50, 54, 84, 85]. Paper 1 of this thesis suggests possible causal inferences for antipsychotic prescribing in the ICU environment. Complex and pragmatic factors such as patient and staff safety and management of hyperactive symptoms nested in a desire to provide high-quality patient care were communicated by healthcare professionals. Based on these findings, it can be proposed that healthcare professionals have robust knowledge of current evidence-based recommendations for antipsychotic prescribing but face diverse clinical circumstances that often lead to antipsychotic medication administration. Acknowledgement and addressing of these factors influencing antipsychotic prescribing are likely essential if targeted and effective strategies for antipsychotic minimization and deprescribing are to be successful.

5.4.2 Well-defined Parameters for Use of Antipsychotic Medications

Antipsychotic medications are prescribed to critically ill patients for several clinical indications beyond delirium. Paper 2 of this thesis enumerated the common alternative indications for which antipsychotics are prescribed within the ICU, demonstrating inconsistent parameters for these prescribing practices. Agitation, sleep, and achievement of sedation were described as alternative indications for antipsychotics. Kim and colleagues identified longitudinal trends in the types and doses of antipsychotics prescribed off-label (i.e., not for primary psychiatric disorders) among post-operative cardiac surgery patients [83]. These longitudinal trends highlighted a lack of antipsychotic prescribing parameters with concerning increases in

quetiapine prescribing, potentially excessive antipsychotic dosing, and substantial hospital-level prescribing variability. Current antipsychotic prescribing practices in the ICU, which are largely for off-label indications, lack parameters for healthcare professionals to help guide safe, appropriate, and time-limited use of antipsychotic medications. A foundational framework of priority clinical indications for antipsychotic prescribing is documented in Paper 3. Parameterizing the use of antipsychotic medications in the ICU in the form of frameworks or decision support tools may reduce clinician variability in treatment decisions related to antipsychotic prescribing, in turn reducing potentially inappropriate antipsychotic prescribing practices [86].

5.4.3 Support During Transitions of Care

Transitions of care constitute a high-risk period during hospitalization where patients who experience critical illness may be continued on potentially inappropriate medications [87]. Critically ill patients may be unable to actively participate in their medical care during these transitions of care due to ongoing delirium, previous sedation exposure, and/or the severity of illness [88, 89]. Medication reconciliation procedures form the cornerstone of identifying potentially inappropriate and high-risk medications when critically ill patients transition from the ICU to the hospital ward and home [90]. Medication reconciliation focuses on the deliberate and conscientious interprofessional process of medication management optimization through verification, clarification, and reconciliation of patient medication lists [90, 91]. Paper 1 in this thesis highlights the complexity of antipsychotic prescribing practices with both individual, patient, and system-level factors influencing the prescribing and deprescribing of antipsychotic medications. The findings provide qualitative evidence to support the results of a recent systematic review that suggest the efficacy of medication reconciliation alone as a mechanism to identify potentially inappropriate medications such as antipsychotics may be insufficient to effectively identify, plan, and implement deprescribing of these medications at transitions of care

[90]. The recommendations from Paper 3 support the use of multicomponent interventions that engage all healthcare team members in bidirectional communication when addressing antipsychotic medication prescribing and deprescribing – a finding further supported by Dautzenberg and colleagues in their systematic review suggesting a decreased risk of hospital readmission in older adults when combined co-interventions focused on medication reconciliation, patient education, professional education, and transitional care were utilized [92]. Merging bidirectional communication tools between healthcare team members as well as patients and their families with medication reconciliation may provide an effective framework to establish appropriate antipsychotic minimization and deprescribing recommendations at transitions of care.

5.5 Directions for Future Research

The current scope of the research conducted in this thesis provides foundational understanding of the important facilitators and barriers relevant to antipsychotic medication prescribing practices in critically ill adult patients. Leveraging various methodologies, the studies in this thesis utilized tailored knowledge on current antipsychotic prescribing guidelines to sequentially identify, describe, and adapt this knowledge to the Canadian context to best understand the barriers to antipsychotic minimization and deprescribing [93, 94]. The following two sections present directions for future research to improve how high-risk sedative pharmacologic agents, which include antipsychotics, are responsibly prescribed to critically ill patients.

5.5.1 Building of Care Pathways for Antipsychotic Use

To optimize the way in which non-pharmacologic interventions (i.e., ABCDEF bundle) for the prevention and management of delirium and/or agitation are implemented, care pathways that provide guidance on appropriate circumstances for time-limited use of antipsychotics and subsequent deprescribing strategies should be incorporated into current conventional non-pharmacologic care bundles [19]. Systematic efforts to encourage adoption of care pathways for antipsychotic prescribing and deprescribing may augment the efforts and positive outcomes from non-pharmacologic care bundles for delirium and agitation prevention and management. Substantial variation exists in antipsychotic prescribing practices that are rooted in little evidence to justify such heterogeneous prescribing across healthcare professionals. Future research should aim to formalize and explicitly define antipsychotic prescribing care pathways for clinical indications where equipoise is likely to continue for years to come as a potential solution to reduce overprescribing and the inappropriate long-term continuation of antipsychotics.

5.5.2 Application of Methodology to Other Sedation Practices

Several additional high-risk sedative medications including benzodiazepines and opioids are commonly utilized within the ICU to achieve sedation and manage agitation symptoms related to delirium. Current guidelines, which focus on implementation of non-pharmacologic interventions (i.e., ABCDEF bundle), endorse avoiding benzodiazepine medications and judicious prescribing of opioid medications [20]. It has been well-established that benzodiazepine use is associated with an increased risk of delirium incidence, longer delirium duration, and prolonged mechanical ventilation [15, 95, 96]. Further, recent observational and interventional studies have identified an association between the administration of opioids and a subsequent increased risk of delirium incidence [14, 97]. Avoidance of deep sedation that can

result from the accumulation of lipophilic sedative infusions (e.g., fentanyl, midazolam) reduces the risk of delirium and shortens duration of mechanical ventilation [95, 98]. Recent clinical challenges related to the COVID-19 pandemic and the management of severe ARDS has exacerbated the use of deep sedation with benzodiazepines and opioids, risking the loss of progress achieved from years of advocacy for non-pharmacologic interventions for delirium prevention [99]. Future research should apply comparable methodologies as this thesis to address highly complex issues surrounding appropriateness of sedation prescribing targeting the development of applicable and scalable sedation care pathways for critically ill patients to help guide clinician decision-making.

5.6 Recommendations for the Field

Converging on the pharmacologic management of delirium, agitation, and sleep disturbances, the field of critical care medicine should focus on three specific areas to better define how, when, and if antipsychotics should be employed in the care of critically ill patients. First, refinement and distinction of hyperactive delirium, currently characterized by psychomotor agitation, sleep disturbances, and aggression, is necessary from hypoactive delirium to better understand precise clinical phenotypes to guide specific pharmacologic interventions for patients that experience this clinical syndrome. Second, current antipsychotic medication prescribing for delirium, agitation, and sleep disturbances is informed by low-quality evidence for some of the most common antipsychotics prescribed to critically ill patients. These evidence gaps would benefit from large-scale interventional studies to rigorously evaluate the short-term and long-term patient-level outcomes and potential harms associated with ongoing antipsychotic use. Third, knowledge translation of delirium research has lagged behind knowledge generation and contributes to the arbitrary application of evidence for antipsychotic prescribing in clinical

practice. Embracing implementation science for rapid translation of delirium research into clinical practice is needed to innovate complex care pathways integrating pharmacologic and non-pharmacologic evidence for the management of delirium and agitation to streamline clinical practice across healthcare professionals. The following three sections present recommendations for the field of critical care to enhance and improve appropriate use of antipsychotic medications in critically ill patients, particularly for those patients who experience delirium.

5.6.1 Precision in Delirium Subtypes and Pharmacologic Interventions

Delirium has been traditionally classified by motoric subtypes in an attempt to unify the constellation of clinical symptoms experienced by patients [100]. Evolving literature in the long-term cognitive and functional outcomes of those critically ill patients that experience the hyperactive delirium subtype and psychomotor agitation during hospitalization suggest distinct prognostic features compared to hypoactive and mixed delirium subtypes [101, 102]. Patients who experience isolated hyperactive delirium display a lower risk of developing long-term global cognitive and executive functioning deficits [101]. On the other hand, patients who experience mixed delirium with episodes of both hyperactive and hypoactive symptoms appear to be at the highest risk of mortality, longer delirium duration, and increased length of hospital stay [103]. The multidimensional nature of delirium, its temporal fluctuance, and still imprecise research instruments to accurately categorize and capture the nuances of delirium subtypes leaves distinct heterogeneity in the diagnosis of delirium both clinically and in research. Shifting toward new broader definitions of delirium subtypes that encapsulate both important biomarkers and risk factors while de-emphasizing current focus on psychomotor symptoms has been suggested as a mechanism to develop opportunities for linking delirium as a syndrome to focused non-pharmacologic and pharmacologic interventions [104].

Critically ill patients with mixed delirium, the most frequently reported delirium subtype, receive more pharmacologic interventions with antipsychotic medications than other delirium subtypes [103]. According to one recent systematic review evaluating antipsychotic prescribing practices by delirium subtype, over one-half of patients with mixed delirium receive an antipsychotic medication during their ICU admission [103]. Although patients may be perceived as appearing more comfortable after treatment with antipsychotic medications, these patients may simply be cycling into hypoactive delirium due to sedative medication administration. With the large proportion of patients with mixed delirium receiving antipsychotic medications, the question is whether medication administration could be associated with the increased mortality and increased length of stay observed in this delirium subtype? Current antipsychotic prescribing practices mirror the imprecise understanding and definition of delirium subtypes with healthcare professionals left with no effective pharmacologic options that address the underlying pathophysiology of delirium. Refinement of current delirium subtypes with new models to improve delirium phenotyping reflecting both clinical and neurobiological pathology are necessary to target patients where antipsychotics may be appropriate and limit inappropriate antipsychotic administration in those where it is not.

5.6.2 Large-Scale Study of the Efficacy and Safety of Antipsychotic Medications

Current guidelines recommend against the routine administration of antipsychotic medications for delirium and agitation [20]. However, these recommendations are conditional with very low to low quality evidence. There is significant heterogeneity in the current available data on several commonly prescribed antipsychotic medications within the ICU. Randomized control trials on several antipsychotics have methodological concerns related to either the sample size, study population, or instruments used to measure delirium incidence [44, 47, 105]. Since the publication of the current iteration of the Society of Critical Care Medicine Clinical Practice Guidelines on the Prevention and Management of Pain, Agitation/Sedation, Delirium,

Immobility, and Sleep Disruption, few additional large-scale randomized studies have been completed to evaluate the efficacy of antipsychotic medications for the treatment of delirium, agitation, and sleep disturbances [20, 41]. Evaluation of pharmacotherapeutics for delirium and sleep has shifted to alternative sedative agents such as dexmedetomidine [106-109].

Large evidence gaps remain in evaluating the risks and benefits of antipsychotics for the treatment of delirium, agitation, and sleep disturbances. Many studies lack generalizability for the broader critically ill patient population due to restrictive patient inclusion criteria (e.g., inclusion of cardiac surgery or non-critically ill patients only), unblinded study designs, and lack of appropriate comparison control arms (e.g., alternative antipsychotic medication as placebo). Yet these antipsychotic medications continue to form a fundamental practice pattern for healthcare professionals in part due to a lack of high-quality evidence to better inform clinical practice. Further, it is unknown what impact the use of antipsychotics in patients with delirium, agitation, and/or sleep disturbances has on long-term outcomes in critically ill patients. No studies evaluating antipsychotic use for delirium have assessed the long-term cognitive sequelae of their use in this patient population. In non-critically ill patients, long-term antipsychotic use is associated with increased risk for hospitalization and a dose-dependent increase in mortality [110-113]. The contributions of antipsychotics (if any) to the long-term outcomes – cognitive, psychological, and physical – in critically ill patients during their recovery from critical illness warrants further thoughtful evaluation within the field of critical care medicine.

5.6.3 Enhanced Translation of Delirium Research into Clinical Practice

Implementation science studies how healthcare interventions are adopted or not adopted in clinical settings emphasizing the use of complex, multicomponent interventions addressing adaptive challenges to behaviour change [114]. The field aims to identify facilitators and barriers to evidence-based clinical practices using systematic methods to test novel

strategies for implementation [114, 115]. The translation of new scientific discovery, whether they encompass the adoption or de-adoption of clinical interventions, is an active process without which the implementation of clinically effective interventions will otherwise occur via untargeted and uncontrolled mechanisms [114, 116].

To improve antipsychotic prescribing and deprescribing practices and the implementation of other non-pharmacologic practices for the prevention and management of delirium, agitation, and/or sleep disturbances, the field of critical care medicine should consider innovating adaptable and scalable combined care pathways for both the pharmacologic (i.e., antipsychotics) and non-pharmacologic (i.e., ABCDEF bundle) management of delirium, agitation, and sleep. This approach may help streamline clinical practice using current best available evidence while prioritizing quality and patient safety principles. Integrating non-pharmacologic care bundles for delirium (i.e., ABCDEF bundle) with pharmacologic recommendations into clinical decision support tools as a comprehensive conceptual model for implementation may optimize evidence-based practices into clinical care and improve important short-term and long-term patient-centered outcomes [116].

5.7 Conclusions

Some clinical care decisions remain informed by arbitrary, traditional clinical practices with little evidence to support specific decision-making, such as antipsychotic prescribing in critically ill patients with delirium, agitation, and/or sleep disturbances. Variations in prescribing and deprescribing practices are thus common among clinicians and across hospitals and health systems. The findings in this thesis show that even when presented with robust evidence to question traditional prescribing practice patterns, changes to the delivery of care may be slow and fraught with barriers. To move toward more rapid implementation and de-implementation of

evidence-based care, the field of critical care medicine must aim to become a learning healthcare system; a system where researchers, healthcare professionals, patients and their families, and health system leaders are brought together to recognize knowledge and care gaps, integrate research inquiry into clinical practice, and systematically implement best research evidence into clinical care to improve patient outcomes. Engaging in a learning health system will require acknowledging arbitrary variations in clinical practice as an opportunity to evaluate clinical care delivery and to prioritize implementation of appropriate practice changes to improve patient outcomes. The success of such approaches will depend on the willingness of researchers, patients and their families, healthcare professionals, and health systems to engage meaningfully together in all phases of research from study prioritization to clinical implementation.

APPENDIX A. PERMISSION TO INCLUDE PAPER 1 IN THESIS

Dear colleagues,

As one of the final steps in preparing my MSc thesis document, I require your written permission to include our prepared and ready to submit publication titled, "Facilitators and barriers to deprescribing antipsychotic medications in critically ill adult patients: A qualitative study using the Theoretical Domains Framework" in my thesis.

In addition to agreeing for me to include the paper in my thesis, you will also be agreeing for it to be submitted to the University of Calgary Thesis Vault, according to the Faculty of Graduate Studies electronic thesis and dissertations program.

The title of my thesis is: Facilitators and barriers to deprescribing antipsychotic medications in critically ill adult patients at transitions of care.

If you receive multiple emails from me on this matter (i.e., if you are a co-author on more than one of my thesis papers), then I kindly ask that you respond to each email separately, as permission for each paper is required.

Thank you in advance for your response.

Best,
Natalia

Natalia, congrats on your hard work.
Permission granted.
Sincerely, lisa

You have my permission.

Best,
Kirsten

Permission granted!

Dan

Dear Natalia,

You have my permission to submit the publication titled "Facilitators and barriers to deprescribing antipsychotic medications in critically ill adult patients: A qualitative study using the Theoretical Domains Framework" as a paper in your thesis, and for it to be submitted to the UofC Thesis Vault.

Best,
Karla

Dear Natalia,

By way of this email, you have my permission to submit the publication titled "Facilitators and barriers to deprescribing antipsychotic medications in critically ill adult patients: A qualitative study using the Theoretical Domains Framework" as a paper in your thesis and also for it to be submitted to the UofC Thesis Vault.

Best wishes,
Jeanna

Hi Natalia,
You have my permission as well.
Z

Dear Natalia,

You have my permission to submit the publication titled "Facilitators and barriers to deprescribing antipsychotic medications in critically ill adult patients: A qualitative study using the Theoretical Domains Framework" as a paper in your thesis, and for it to be submitted to the UofC Thesis Vault.

Best,
Em

APPENDIX B. PERMISSION TO INCLUDE PAPER 2 IN THESIS

Dear colleagues,

As one of the final steps in preparing my MSc thesis document, I require your written permission to include our prepared and ready to submit publication titled, "A scoping review of perceptions of healthcare professionals on antipsychotic prescribing practices in acute care settings" in my thesis.

In addition to agreeing for me to include the paper in my thesis, you will also be agreeing for it to be submitted to the University of Calgary Thesis Vault, according to the Faculty of Graduate Studies electronic thesis and dissertations program.

The title of my thesis is: Facilitators and barriers to deprescribing antipsychotic medications in critically ill adult patients at transitions of care.

If you receive multiple emails from me on this matter (i.e., if you are a co-author on more than one of my thesis papers), then I kindly ask that you respond to each email separately, as permission for each paper is required.

Thank you in advance for your response.

Best,
Natalia

Hi Natalia,

Whatever you need. Please accept this email as confirmation that I agree.

lisa

Dear Natalia,

Yes, of course. You have my permission.
Congratulations on reaching this stage in your program. Well done!

All best wishes,
Stephana

You have my permission.

Best,
Kirsten

Hello Dr. Jaworska,

You have my permission! I can't wait to read the final product!

Sincerely,
Zara

Permission granted here as well!

Dan

Hi Natalia,

You absolutely have my permission. Congratulations!

Best,
Karla

Hi Natalia,

You have my permission as well.

Z

APPENDIX C. PERMISSION TO INCLUDE PAPER 3 IN THESIS

Dear colleagues,

As one of the final steps in preparing my MSc thesis document, I require your written permission to include our prepared and ready to submit publication titled, "A nationwide modified Delphi consensus process to prioritize experiences and interventions for antipsychotic medication deprescribing among adult patients with critical illness" in my thesis.

In addition to agreeing for me to include the paper in my thesis, you will also be agreeing for it to be submitted to the University of Calgary Thesis Vault, according to the Faculty of Graduate Studies electronic thesis and dissertations program.

The title of my thesis is: Facilitators and barriers to deprescribing antipsychotic medications in critically ill adult patients at transitions of care.

If you receive multiple emails from me on this matter (i.e., if you are a co-author on more than one of my thesis papers), then I kindly ask that you respond to each email separately, as permission for each paper is required.

Thank you in advance for your response.

Best,
Natalia

Hi Natalia, you have my permission to include it in your thesis.

bw,
Geeta

Hi Natalia,

Whatever you need. Please accept this email as confirmation that I agree.

lisa

You have my permission.

Best,
Kirsten

Hi Natalia,

Thanks for your email. Please accept this response as permission to include the Delphi paper in your thesis.

Cheers,
Kira

Permission granted here too!

Dan

Dear Natalia,

You have my permission to the manuscript titled, "A nationwide modified Delphi consensus process to prioritize experiences and interventions for antipsychotic medication deprescribing among adult patients with critical illness" in your thesis. Congratulations on all your hard work!

Best,
Karla

Hi Natalia,

You have my permission as well.

z

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