A multi-methods exploration of shared decision-making, lived experience, and opioid use disorder among emerging adults with anxiety and depression

by

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ABSTRACT

Background

Anxiety/depression are common in emerging adults and may lead to poor coping strategies such as substance use. Shared decision-making (SDM) occurs when clinicians and patients make health decisions together informed by the best available evidence inclusive of the patient's values/preferences. Among adults with chronic diseases (e.g., diabetes), evidence suggests SDM may enhance patient outcomes such as satisfaction with care, health-related quality of life (HRQL) and patient health engagement (PHE). Whether SDM benefits emerging adults with anxiety and/or depression remains to be elucidated.

Objectives

i. To explore whether SDM is associated with patient outcomes such as anxiety/depression, PHE, and HRQL.

ii. To describe the narrative account of emerging adults coping with anxiety/depression.

iii. To investigate whether previous anxiety and/or depressive disorders are associated with subsequent opioid use disorders (OUD).

Methods

Chapter 2: A systematic literature review was conducted exploring whether SDM is associated with clinically relevant outcomes compared to usual care in adults 18-64 years with anxiety/depression. Study eligibility criteria: i) prospectively controlled trials, ii) peer-reviewed and published in English-language.

Chapter 3: A narrative inquiry was conducted exploring the experiences and decision-making preferences of emerging adults coping with anxiety/depression. Data were obtained by conducting unstructured verbal interviews in mental health and primary care settings. The data were transcribed verbatim and analyzed descriptively.

Chapter 4: A cross-sectional study was conducted exploring whether SDM was associated with changes in PHE, HRQL, anxiety/depression in emerging adults (18-29 years) with anxiety/depression. Data were analyzed using non-parametric statistical methods.

Chapter 5: An age/sex matched case-control study was conducted exploring whether previously diagnosed anxiety and/or depressive disorders were associated with subsequent OUD in emerging adults (18-25 years). Administrative health data were analyzed, and adjusted odds ratios were calculated using conditional logistic regression.

Results

Chapter 2: Six randomized controlled trials (N=1,834 participants, 18-64 years) were included. SDM improved the following outcomes: patient satisfaction (n=3 studies), adequate treatment for depression (n=3 studies), decrease in anxiety symptom severity (n=1 studies), patient involvement in decision-making (n=3 studies). No studies or data of emerging adults were obtained. Quality of the evidence ranged from low to moderate.

Chapter 3: Twelve emerging adults with anxiety and/or depression were interviewed. Common narratives included: i) feeling overwhelmed, ii) social/peer pressure, iii) withdrawing socially, iv) self-medicating with substances/alcohol, v) seeking mental health care as a last resort, vi) positive social support may facilitate seeking treatment, vi) increased involvement in decision-making may impact satisfaction with care and treatment adherence.

Chapter 4: Thirty-one healthcare providers and 42 emerging adult patients (22% male) were recruited from six primary care and eight mental health settings in Alberta. Excellent use of SDM during an initial consultation was not associated with PHE, anxiety/depression or HRQL compared to acceptable/unacceptable SDM. P

Chapter 5: We identified N=1,848 cases and N=7,392 controls. Later OUD was associated with the following preexisting disorders: anxiety, aOR=2.53 (95% CI=2.16 – 2.96); depression, aOR=2.20 (95% CI=1.80 – 2.70); and concurrent anxiety and depression, aOR 1.94 (95% CI=1.56 – 2.40). Post-hoc analyses revealed subsequent OUD diagnoses were associated with the following preexisting concurrent disorders: anxiety and alcohol, aOR=1.94 (95% CI=1.56 – 2.40); depression and alcohol, aOR=6.47 (95% CI=4.73 = 8.84); anxiety, depression and alcohol, aOR=6.09 (95% CI=4.41 – 8.42).

Discussion

It is unknown whether the use of SDM during clinic visits may enhance patient outcomes in emerging adults with anxiety and/or depression. The literature obtained from the systematic review suggests SDM may either improve or provide no benefit on patient-reported outcomes in adults with depressive disorders. Our cross-sectional study found no relationship between SDM and HRQL, PHE, and anxiety/depression in emerging adults. The obtained qualitative evidence suggests i) emerging adults may have diverse experiences, expectations, and values for managing symptoms of anxiety/depression, ii) inclusive approaches to care such as SDM may be valued. Previous anxiety/depression in youth is associated with developing subsequent OUD. Alcohol-related disorders in addition to anxiety/depression considerably amplify the risk of OUD. More longitudinal research is needed to determine whether SDM provides benefit for emerging adults with mental health concerns. More research is urgent needed to reduce the burden of

anxiety/depression and substance use in youth. More research around person-centred care and SDM are warranted in people with anxiety disorders and emerging adults.

PREFACE

Chapter 2

All authors have made significant intellectual contribution to the development of this manuscript. TM and SV developed the research questions and methods. TM produced the first draft of the manuscript. CS, KO, AA, RL, XL assisted in refinement of the research questions and revisions of the manuscript. TM and a health research librarian with systematic review expertise designed the search strategy and performed the database searches. TM and CS screened, extracted and analyzed the data. SV has expertise in systematic reviews and provided detailed feedback on all manuscript drafts. All authors have contributed substantially to the conception, acquisition, analysis, interpretation of data, and have approved the final version of this manuscript.

Chapter 3

The first author and the senior author developed the research questions and methods. The co-authors provided substantial input into the development of the research questions and methods. The first author collected and analyzed the data and drafted the manuscript. Each author provided feedback drafts of the manuscript. All authors approved the final version of this manuscript.

Chapter 4

All authors have made significant intellectual contributions to the development of this manuscript. TM, KO, and SV developed the initial research questions and methods. KO, AA, RL, XL assisted in refinement of the research questions, development of the methods, and revisions of the manuscript. TM analyzed the data. All authors have provided substantial intellectual input and have approved the final version of this manuscript.

Chapter 5

TM, KO and RL had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. TM, RL, KO, SV developed the research questions and methods. TM produced the initial draft of the manuscript. AA, XL assisted in refinement of the research questions, methods, interpretation and revisions of the manuscript. EY extracted, cleaned the data and provided substantial revisions to the methods and manuscript. All

authors have contributed substantially to the conception, acquisition, analysis, interpretation of data, and have approved the final version of this manuscript.

Chapter 7

TM developed the research questions, analyzed the data and produced the first draft of the manuscript. MH analyzed the data and helped produce the first draft of the manuscript. ENK, KO assisted in the development of the research questions, arbitrated disagreements, and revisions of the manuscript. TM and ENK consulted public health subject matter experts in the USA. AA-A, RT, JNS, and KR provided substantial clinical expertise and edited the manuscript. SV has expertise in conducting systematic reviews and provided detailed feedback and guidance at each stage of the review process. All authors contributed substantially to conception, design, analysis and interpretation of this work. All authors have approved the final version of this manuscript.

DEDICATION

This dissertation is dedicated to the many lives lost that have impacted me and motivated me in my life. Your spirit drives me to never ever quit. To my dad, Richard D. Marshall (1962–2011), my grandfather, Sgt. Albert S. Marshall (1920–1975), my grandfather, Robert B. McKinnon (1927–2018), my grandmother, Bettye McKinnon (1931–2020), my aunt, Betsy McKinnon Wells (1958–2008), my stepbrother, Taylor Webster (1991–2010), and my friend, Jared Neal (1991–2019). This dissertation is also dedicated to the families and friends of those who have lost loved ones due to mental health and/or substance use.

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LIST OF ABBREVIATIONS

HRQL	Health-Related Quality of Life
OUD	Opioid Use Disorder
PHE	Patient Health Engagement
RCT	Randomized Controlled Trial
SDM	Shared Decision-Making
WHO	World Health Organization

CHAPTER 1: INTRODUCTION

1.1 Background

Over the past decade, mental health disorders (including substance and alcohol use disorders) have posed an increasing burden on the healthcare system.[1] In 2010, mental health disorders were responsible for approximately $2.5 trillion in personal and health system costs[2], and these costs are expected to rise 240% to $6 trillion by 2030.[3] In 2016, mental health disorders impacted over 1 billion people worldwide – nearly one-eighth of the world's total population.[4,5] The World Health Organization (WHO) attributes 10% of the total global disease burden to mental health disorders measured by disability-adjusted life years[3], which sum years of life lost due to premature mortality and disability.[6] The prevalence and burden of anxiety and depressive disorders (including conditions such as posttraumatic stress disorder) have increased in the wake of the COVID-19 pandemic[7], and will likely remain global public health priorities in the coming years.[8,9]

Depressive disorders may be the most burdensome of all mental health disorders, globally.[2] Depressive disorders, particularly when left untreated, pose a substantial risk for suicide, contributing to approximately 800,000 deaths per year, globally.[10] The global prevalence rate of depressive disorders is estimated to be around 4.4%, and more common in women than men by a ratio of nearly 2 to 1.[11] Evidence suggests that depressive disorders most commonly onset during young adulthood, between the ages of 18-29 years.[12] The WHO characterizes depression as feelings of "sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, feelings of tiredness, and poor concentration that substantially impairs an individual's ability to function at work or school or cope with daily life."[2] Depressive disorders are comprised of two main subcategories: i) major depressive disorder/depressive episodes; and ii) dysthymia. Major depressive disorder is characterized by anhedonia and decreased energy for a prolonged period, and severity specifiers range from mild, moderate, to severe.[2] Dysthymia is a more chronic form of mild depression, typically less severe than major depressive disorder, but longer in duration.[2] In contrast, bipolar disorder is characterized by the presence of both manic and depressive episodes and is categorized as a mood disorder rather than a depressive disorder.[2]

Anxiety disorders pose a tremendous burden on population mental health, rivaling the deleterious impacts of depression.[13]A systematic review estimated the global prevalence of anxiety disorders

to be higher than depressive disorders, approximately 7.3% (SD=4.8-10.9) after adjusting for methodological heterogeneity.[14] Anxiety disorders are thought to contribute substantially to increased unemployment rates and loss of economic output.[2,15] The World Health Organization (WHO) characterizes anxiety disorders as "a group of mental disorders characterized by feelings of anxiety and fear, including generalized anxiety disorder (GAD), panic disorder, phobias, social anxiety disorder, obsessive-compulsive disorder (OCD) and posttraumatic stress disorder (PTSD)."[2] Anxiety disorders range from mild, moderate, to severe in intensity and typically persist over time. Similarly with depressive disorders, anxiety disorders typically onset during late adolescence or young adulthood, most commonly between 17 and 26 years of age.[16] However, anxiety disorders such as specific phobia, social phobia, and social anxiety disorders commonly onset before 15 years of age, while conditions such as panic disorder, obsessive-compulsive disorder and generalized anxiety disorder typically onset later in young adulthood, between 21 and 35 years of age. In contrast with depression, anxiety disorders tend to onset at similar ages and incidence rates are similar between males and females.[16]

Anxiety and depressive disorders commonly co-occur, often complicating diagnosis and treatment.[17] Epidemiological evidence suggests that anxiety disorders such as generalized anxiety disorder commonly precede depressive disorders by 2-4 years and increase the risk of depressive disorders.[16,18] A study of 106 participants found that adolescents with co-occurring anxiety and major depressive disorder tended to be older and have more severe anxiety symptoms.[18] When inadequately treated, these conditions are associated with the onset of a plethora of health complications such as obesity, diabetes, hypertension, cardiovascular disease, and substance use disorders.[19,20] Substance use disorders, and opioid use disorder in particular, are a public health issue of special concern/focus in this dissertation due rising morbidity and mortality rates and high comorbidity rates with common psychiatric disorders such as anxiety and depression.[21-23] It is estimated that 92.5% of individuals with OUD meet criteria for at least one psychiatric disorder, and risk of psychiatric comorbidity increases as age of first opioid misuse decreases.[24] Better understanding of the relationship between anxiety, depression and opioid use disorder may inform clinical and public health policy efforts to mitigate the deleterious impact of these conditions in emerging adults.

1.2 Research in the context of the drug overdose crisis

A drug overdose epidemic has plagued North America since the beginning of the millennium and has substantially accelerated in severity since 2015.[21-23] Of particular concern is the rapidly growing proportion of deaths involving potentially illicitly manufactured (and purchased) opioids such as fentanyl and carfentanil.[23,25,26] These drugs, especially when misused non-medically and injected intravenously, pose a heightened risk of death in comparison with the oral use of less potent opioids such as morphine, methadone, or hydromorphone.[27-31] Misuse of fentanyl and its analogues pose a heightened risk of respiratory depression facilitated by its narrow therapeutic index (i.e., the dose required to achieve the desired euphoric effect is close to the lethal dose).[31,32] Complicating matters, fentanyl has a high affinity for mu-opioid receptors, facilitating rapid tolerance, physical dependence, and more painful withdrawal symptoms, substantially increasing the risk of opioid use disorder (OUD). OUD is defined as a compulsive, nonmedical use of opioids (e.g., heroin, fentanyl) that persists despite adverse consequences to daily life and/or functioning for at least 6-months.[33,34] It is estimated that between 34.3 – 47.9 million people, and 40.5 people meet the criteria for OUD worldwide. In 2017, between 105,800 – 113,600 people died from opioid-related overdoses during a 12-month period.[35] Beyond overdose deaths, nonfatal overdoses often lead to significant morbidity including hospitalization, coma, and permanent disability.[36] OUD is strongly associated with injection drug use, contributing to a high risk of secondary infections such as endocarditis, hepatitis C and HIV.[37]

1.3 Mental health and substance use in emerging adults

Over the last several decades, emerging adulthood has become accepted as a unique stage of psychosocial development, distinct from adolescence and adulthood. Emerging adulthood does not have an established age range and has been inconsistently defined throughout the peer-reviewed literature. The theory of emerging adulthood is thought to be more related to psychosocial and environmental characteristics such as housing, career/income, student and marital status rather than numerical age.[38,39] For simplicity, some studies define emerging adulthood as 18-25 years[38], while others are more inclusive and consider those 18-29 years to be emerging adults.[39]

Erikson' psychosocial stage theory describes the psychological stages of identity and ego development which commonly occur during adolescence and emerging adulthood.[40,41] Often, people in this age range place high value on building strong social relationships and "fitting in"--

to help protect self-esteem and the ego.[40,41] Building on these works, Arnett, in 2000, first coined the term "emerging adulthood", and characterized emerging adulthood as: "(a) the age of identity explorations, (b) the age of feeling in between, (c) the age of possibilities, (d) the self-focused age, and (e) the age of instability."[38,40-42] The theory of emerging adulthood may also be understood from the lens of attachment theory, which characterizes phenomena related to abrupt changes in the parent-child relationship which commonly occur during late adolescence and emerging adulthood.[40,43] Evidence from psychological sciences have supported this theory showing that emerging adults are more likely to value autonomy, independence, and novel social experiences compared to adolescents living at home and young adults who have steady employment, etc.[38,39,44,45]

Additionally, neuroimaging data suggest the brains of emerging adults may be more similar to adolescents than older adults.[46] For example, magnetic resonance imaging studies have revealed that cortical maturation may not finalize until at least 25 years of age.[47] Cortical maturation is characterized by pruning of unused cortical grey matter neurons while increasing white matter connectivity between essential brain regions.[47,48] Importantly, key brain regions critical for decision-making and emotional regulation such as the prefrontal cortex continue to develop/mature during this period.[47 48]

The theory of emerging adulthood may be best characterized by the psychosocial challenges experienced during this period.[49] For instance, emerging adults commonly transition from their caregiver's household and begin to pursue life independently.[50] During this time, increased occupational, financial and/or academic challenges onset, while often pursuing novel romantic and social experiences.[49] Over the past several decades, increased environmental pressures have been placed on emerging adults, while support services have remained scarce and/or underutilized.[51,52] For example, there has been a global shift from an industrial-based economy common in the 20th century to a more technology-based global economy[53] often requiring more education and training to obtain a well-paying employment potentially leading to lower income and more socioeconomic instability during the emerging adulthood years.[53]

1.4 Person-centred mental healthcare: a theoretical framework

The World Health Organization (WHO) has widely recommended enhanced individual, family, and community involvement in health-related decision making in the form of person-centred care

to mitigate the global burden of chronic conditions.[54,55] Person-centred care (also known as patient or client-centred care) is best conceptualized as a collaborative approaches to comprehensive care tailored to an individual's unique needs, involving a therapeutic relationship between healthcare providers and patients – in addition to their families or caregivers, if desired.[55-57] A systematic review in 2012 suggested that person-centred approaches to care may improve the quality of care in the domains of self-management and satisfaction with care,[57] which may reduce downstream health system costs.[57,58] Evidence-based and person-centred care is thought by many scholars to be largely based on the use of shared decision-making (SDM) between healthcare providers and patients.[59-61]

From 2010-2012, Elwyn and colleagues developed and implemented a model to promote SDM in clinical practice in the United Kingdom.[62] The authors articulated SDM as "an approach where clinicians and patients make health decisions together informed by the best-available evidence."[62] SDM is distinct from other decision-making styles such as the informed choice model and traditional decision making models.[62-68] The informed choice model promotes fully independent/autonomous patient decision-making and may be facilitated by interventions such as web-based decision aids (i.e., decision support tools) in the absence of healthcare provider input.[63,65] Traditional, sometimes viewed as paternalistic, decision-making styles rely heavily on clinician expertise to guide decision-making for the patient.[65] SDM conceptually falls in between these two former models and encourages negotiation, patient engagement, and knowledge exchange between the clinician and patient.[62,66,67,69]

Previous systematic reviews have demonstrated empirical support of SDM for improving patient-reported outcomes with little to no evidence of harm, particularly in the arena of primary care and chronic disease management.[70] Advantages of SDM may include enhanced therapeutic and collaborative clinician-patient relationships (e.g., therapeutic alliance and trust) and improving satisfaction with care which may promote downstream outcomes such increased early identification and treatment, increased treatment adherence, and reduced relapse rates.[70] More recent research suggests SDM may be feasible/applicable and beneficial in psychiatric and mental healthcare settings[66,67,69,71-73] A recent systematic review has shown the SDM may be applicable even in patients with serious mental illness such as schizophrenia, and patients in psychiatric care may have unique decision-making needs.[74] Moreover, a systematic review in 2018 showed that

the use of SDM, when facilitated by decision aids, may improve satisfaction and engagement in the decision-making process in adult patients with a variety of mood disorders.[72] Limitations of SDM may include the concern that shifting complex medical decision-making to patients may encourage uninformed choices leading to harm or no benefit. Additionally, there are concerns whether SDM takes too much time, and whether it is appropriate in youth or individuals with serious mental illness.[64] Furthermore, some evidence suggests that not everyone may desire or respond to this approach. For example, individuals with cognitive impairments may be less likely to engage in SDM, leading to ethical concerns that these individuals may not be able to make complex health decisions that may be in their best interest.[75]

1.5 Shared decision-making: a good fit for emerging adults with mental health concerns?

Mental disorders such as anxiety, depression, and substance use disorders most commonly onset during emerging adulthood and are most common in this age group.[52,76-78] Emerging adults are the least likely to seek and stay engaged in professional mental health services[45,51,79,80] which may be linked to poor outcomes and high health system costs.[79,81] Recent systematic reviews suggest that using positive reinforcement, as opposed to punitive approaches, may be useful for improving outcomes in emerging adults with chronic conditions and/or engaged in high-risk behaviours such as substance use (including alcohol and tobacco).[82] Little is known about: i) the specific needs and values of emerging adults with anxiety and depression; ii) to what extent emerging adults prefer to be involved in decision-making; and iii) whether more person-centred approaches to care such as SDM might improve outcomes.

1.6 Overall aims of the dissertation

Broadly, I aimed to explore whether SDM is associated with clinically relevant outcomes such as patient engagement, quality of life and symptoms of anxiety and depression in emerging adults. Additionally, I aimed to explore any connection to the ongoing overdose crisis by specifically investigating whether there is a temporal association between anxiety, depression, and OUD in emerging adults. This dissertation aims to address important gaps in the evidence, provide next steps for research and insights for service development and policy. The target population of this dissertation focused on emerging adults with mental health conditions such as anxiety, depression, and OUD.

1.7 Specific study objectives

Study 1: To systematically review the impact of SDM on clinically relevant outcomes in adults (18-64 years) with anxiety or depressive disorders and perform a subgroup analysis of any relevant studies of emerging adults.

Study 2: To explore how emerging adults with anxiety and/or depression prefer to make mental health-related decisions, including the decision to seek professional care and engage/collaborate with clinicians in decision-making.

Study 3: To explore whether the quality of SDM during a clinic visit is associated with patient engagement in emerging adults.

Study 4: To investigate whether previously diagnosed anxiety and/or depressive disorders are associated with subsequent OUD in emerging adults.

Study 5 (appendix): To establish the breadth and depth of the relevant scientific literature related to SDM in the treatment of OUD in adults (≥18 years), and summarize the main findings according to relevant patient health and treatment-related outcomes.

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CHAPTER 2: The impact of shared decision-making in the treatment of anxiety and depressive disorders: A systematic review

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2.1 ABSTRACT

Background: Anxiety and depressive disorders are prevalent and costly conditions globally. Shared decision-making (SDM) involves including patient's values and preferences into health decisions and has shown promise for improving patient outcomes.

Aim: To determine whether SDM impacts clinically relevant outcomes in adults (18-64 years) with anxiety and/or depressive disorders.

Method: A systematic review was conducted. Five electronic health databases were searched from database inception until August 2019. Only prospective, controlled trials comparing SDM to a control condition (e.g., usual care) in adults 18-64 years were included. The Cochrane Risk of Bias tool was used to assess risk of bias; GRADE was used to assess the quality of evidence. Two reviewers independently conducted each stage of the review process.

Results: Six randomized controlled trials (N=1,834 participants, 18-64 years) comparing SDM to treatment as usual control groups were included. SDM improved patient satisfaction in three studies. Patients engaged in SDM plus collaborative care were more likely to receive adequate treatment for depression in three studies. SDM was associated with a decrease in anxiety in one study. SDM increased patient involvement in decision-making in three studies. SDM did not increase consultation time in two studies. Due to the lack of blinded interventions and outcome assessment, the included studies were at moderate risk of bias. The certainty of evidence ranged from low to moderate.

Conclusions: SDM shows promise for enhancing the quality of care for patients with anxiety and depressive disorders but appears unlikely to directly impact symptoms of depression. SDM appears to be understudied in patients with anxiety disorders and in emerging adults. A consistent definition and measurement of SDM is needed in future research.

Keywords: Decision-making, shared; patient-centered care; anxiety disorders; depressive disorder; depression; adults; young adult

2.2 INTRODUCTION

Anxiety and depressive disorders are among the most common mental health conditions worldwide, and are increasingly contributing to the global disease burden.[1, 2] From 2005 to 2015, The World Health Organization reported that the global prevalence of anxiety disorders increased by 14.9%, impacting over 264 million people or approximately 3.6% of the world's population.[1] In the same period, the prevalence of depressive disorders increased by over 50%, affecting over 300 million people or approximately 4.4% of the world's population.[1] More recently, the COVID-19 pandemic has even further accelerated the global mental health crisis, sharply increasing the incidence rates of anxiety and depression.[3] For example, in the United States, the prevalence of anxiety and depressive disorders increased by nearly threefold during 2020, in comparison to 2019.[4] Additionally, anxiety and depressive disorders have long contributed to high health system costs, estimated at nearly $1.15 trillion USD per year, in 2016[1, 3 2] Improving the quality of care for people with anxiety and depressive disorders may substantially reduce the economic burden associated with these conditions.[5, 6] For instance, authors of a recent study demonstrated that for every $1 USD invested into improving the quality of care for anxiety and depressive disorders, a return of $4 USD in global health savings could be expected.[2]

To combat the global burden of chronic diseases, the World Health Organization (WHO) has recently recommended people-centred, evidence-informed, and integrated approaches to service delivery in primary care and mental health care systems world-wide.[7] WHO defines people-centred health services as "an approach to care that consciously adopts the perspectives of individuals, families, and communities and sees them as participants as well as beneficiaries of trust health systems that respond to their needs and preferences in human and holistic ways."[7] WHO further suggests that it is essential that that people have the education/information and support needed to make decisions and participate in their own care.[7] Authors of a systematic review in 2013 found that person-centred (i.e., patient-centred) approaches to care improve self-management of care, and increase patient satisfaction.[8] Increase of self-management of care is thought to increase primary prevention of chronic diseases and reduce the overall burden of these conditions.[8, 9]

Scholars have recommended that the use of shared decision-making (SDM) during clinical decisions may facilitate these public health goals.[10, 11] While there is no universally accepted definition for SDM, Elwyn *et al.,* (2012) described SDM as "an approach where clinicians and

patients share the best available evidence when faced with the task of making decisions, and where patients are supported to consider options to achieve informed preferences."[12] Evidence is emerging in support of SDM for improving patient outcomes. In 2015, Shay & Lafata systematically reviewed the literature and found SDM was most likely to impact "affective-cognitive" outcomes such as patient satisfaction and decisional conflict in patients, but less likely to impact behavioural or health outcomes.[13] This review included 39 studies and a majority of the studies included patients with chronic diseases in primary care settings.

Despite persistent calls for more collaborative and personalized approaches to mental health care [14, 15], it remains unclear whether SDM is beneficial or appropriate for patients with mental health conditions. Some evidence suggests that patients with anxiety and depressive disorders prefer to be included in treatment decisions.[16] Other evidence suggests that some patients with more severe mental health symptoms (e.g., cognitive deficits) may be more likely to defer their health decision-making to a health care provider or caregiver[17-19]; therefore, SDM may not be suitable. Some scholars have, however, argued that failing to include patients in decision-making may be coercive and unethical.[13]

In 2010, a systematic review was conducted by Duncan *et al*.[20] on the impact of SDM on mental health conditions. Only two studies[21, 22] were found, and one showed an improvement on patient satisfaction, while the other study did not. No evidence of effect on clinical outcomes was observed and no harm was reported. In 2018, Samalin *et al*.[23] systematically reviewed the impact of SDM on mood disorders (dysthymia, major depressive disorder, and bipolar disorder). Fourteen RCTs were included; however, only one study suggested that SDM improved depressive symptoms, patient knowledge, or quality of life. The authors found only three studies that investigated SDM in depressive disorder, and studies of patients with anxiety disorders were excluded. The authors concluded that SDM interventions involving decisions aids may improve patient satisfaction and engagement in decision-making. In 2020, Fisher *et al*.[24] conducted a systematic review of mental health and alcohol use disorder comorbidities and found preliminary evidence (10 studies) that SDM may be acceptable, feasible and beneficial, but more research was suggested. Notably, these three systematic reviews did not specifically evaluate the impact of SDM on anxiety disorders, which people with these conditions may prefer and from which they may derive benefit.[16]

2.2.1 Objective

We systematically reviewed the impact of SDM on clinically relevant outcomes in adults (18-64 years) with anxiety and/or depressive disorders.

2.3 METHODS

2.3.1 Protocol and registration

The protocol for this review is published in the PROSPERO International Prospective Register of Systematic Reviews (www.crd.york.ac.uk/PROSPERO), registration number 126079. The PRISMA Statement[25] was consulted to guide the reporting of this systematic review.

2.3.2 Eligibility criteria

We developed *a priori* inclusion/exclusion criteria based on the PICOS model.[26] (**TABLE 1)**

2.3.2.1 Participants

Only studies of adults (18 years and older) formally diagnosed with either an anxiety and/or depressive disorder according to Diagnostic and Statistics Manual (DSM) criteria were included for analysis. Studies including participants less than 18 years of age were excluded, as pediatric patients often require a proxy decision-maker when making health decisions. [27, 28] Studies of older adults (>64 years) were excluded as this population was outside the scope of this systematic review. Studies of patients with other mental or physical health comorbidities were included, except for several mental illnesses such as bipolar disorder, schizophrenia, or suicidality. Patients mandated to treatment for any reason were excluded.

2.3.2.2 Intervention

Studies that operationally defined and evaluated SDM according to our operational definition derived from Elwyn *et al.*[29] were included for analysis. Specifically, an affirmative answer was required for each of the following questions:

- Did the patient and a healthcare provider make a health decision together, informed by the best available evidence?
- Were patients provided options or choices regarding treatment decisions?
- Were patients' preferences considered during decisions around the course of action?

We excluded studies if patients were not explicitly provided with an opportunity to provide input or make choices regarding their treatment plan. Studies were also excluded if no health care provider was available to answer questions or make decisions collaboratively with the patient (e.g., studies using web-based decision aids where a health care provider was not present). In cases where it was unclear if SDM was used, the corresponding author of the study was contacted to verify. If the author did not reply, the study was to be excluded.

2.3.2.3 Control

Only studies that had a control or comparison group (e.g., active controls, sham controls, treatment-as-usual care) were included in this review.

2.3.2.4 Outcomes

Studies with any clinically relevant patient outcome were included in this review (e.g., symptom severity, treatment adherence, health-related quality of life, decisional conflict, patient engagement, patient knowledge, patient satisfaction, consultation time). Studies of health care provider outcomes were excluded.

2.3.2.5 Study type

Only prospective controlled trials published in peer-reviewed medical journals were considered for inclusion.

2.3.3 Information sources

The search strategy was developed and conducted in consultation with a health research librarian who is an expert in systematic review searches. We comprehensively searched MEDLINE, EMBASE, PsycINFO, Cochrane Database for Controlled Trials, and the Cochrane Database for Systematic Reviews from database inception until August 18, 2019. Reference lists of included texts were searched to ensure any remaining relevant articles were identified. Study authors were contacted in case of any missing data. Due to feasibility concerns, only studies published in English-language were considered.

2.3.4 Search strategy

To develop a comprehensive search for all SDM based studies, we pilot-tested a search strategy that employed free-text MeSH subject headings inclusive of terms related to SDM derived from a recent scoping review on SDM.[30] We searched the subject headings "decision-making" and "shared decision-making" and we included additional terms included such as "patient preference" "consumer preference", "patient participation", and "decision support", etc. We also included terms such as "anxiety", "anxiety disorder", "depression", "dysthymic disorder" and "depressive disorder" as our main search terms for anxiety and depression. No search filter for age was used. The preliminary MEDLINE search of studies related to SDM in adults with anxiety and/or depression can be found in (**SUPPLEMENTARY FILE 1**).

2.3.5 Study selection

Endnote (Version X9, Clarivate Analytics) was used to manage the references and full-text pdfs. One reviewer screened the titles and abstract of articles obtained from the database and from the hand searches for eligibility, and another reviewer screened the excluded articles to ensure that relevant articles were not inadvertently discarded. Two reviewers then independently reviewed the full text of each article to assess the inclusion/exclusion criteria. A third reviewer was consulted to arbitrate any disagreements. The selection process is presented in a PRISMA flow diagram in **FIGURE 1**, and reasons for exclusion of any ineligible full-text article are provided.

2.3.6 Data extraction

The included references were exported into a Microsoft Excel spreadsheet to complete the data extraction process. We developed and pilot-tested the data extraction form *a priori* using two randomly selected studies (18/11/19). Two reviewers then independently extracted data from the remaining included studies. We contacted the corresponding authors of the included studies to request any missing data. Any discrepancies in data extraction between the reviewers were resolved by consensus.

2.3.7 Data items

We extracted the following relevant variables: (i) bibliographic information (e.g., first author, title, year of publication, and country); (ii) general study characteristics (e.g., study objectives, study

design, setting, duration, and data collection information); (iii) participant characteristics (e.g., number of patients, number of health care providers, age range, mean age, sex, diagnosis); (iv) methodological characteristics (e.g., number patients allocated to intervention and control, description of intervention, description of control, description of SDM measurement, reported outcomes); (iv) main findings (e.g., effect size, p value, drop-outs, adverse events, author's conclusion and limitations).

2.3.8 Risk of bias within studies

We used the Cochrane Risk of Bias tool for Randomized Controlled Trials[31] to assess the risk of bias for any included RCTs. Two authors independently assessed the risk of bias for each study, and disagreements were resolved by discussion. The results of the risk of bias assessment are presented in **FIGURE 2** and were produced in RevMan version 5.4. The quality of the outcome evidence was assessed by two independent reviewers using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE)[32] tool and reported in **TABLE 4**. A third reviewer was available to arbitrate any disagreements.

2.3.9 Risk of bias across studies

An assessment of publication bias was planned by using a funnel plot, if feasible.

2.3.10 Synthesis of results

A meta-analysis was planned, if a sufficient number of clinically homogenous articles were retrieved.

2.3.11 Additional analyses

Three subgroup analyses were conducted.

i) A subgroup analysis of studies of emerging adults (individuals 18-25 years) was planned *a priori.* Corresponding authors of the included studies were contacted to request data on this age group when possible. This age group was selected because there is reason to suspect that emerging adults may be more receptive to SDM compared to older adults.[33, 34] For example, emerging adults have shown to be more likely to prefer autonomy in health decision-making and self-management of mental

health symptoms.[20, 23] Moreover, anxiety and depressive disorders are widespread globally and are becoming increasingly common in this age group[35], but seldom receive timely and adequate care.[35, 36]

ii) Studies of collaborative care involving SDM were compared to SDM interventions without collaborative care in a post hoc analysis. Collaborative care is considered a patient-centred approach to care involving the use of a multidisciplinary behavioural health care team, typically led by a primary health care provider.[37-39] Collaborative care typically recommends incorporating patient goals into the treatment plan, but may not explicitly recommend or measure SDM.[40] Although, to our knowledge, SDM is not considered an essential aspect of collaborative care, some studies involving collaborative care report making health decisions that are similar or consistent with SDM as defined by Elwyn *et al*.[29]

iii) Studies of SDM facilitated by decision aids were analyzed separately in a post hoc analysis. This analysis may be useful since it is unclear whether decision aids enhance the impact of SDM. Some research suggests that SDM does not require the use of a physical decision aid to be effective.[41] Other studies have suggested that decision aids may promote SDM[42] and have been recommended by Elwyn *et al.*[12] to facilitate evidence-based decision-making while deliberating in SDM.

2.4 RESULTS

2.4.1 Study selection

FIGURE 1 illustrates the study selection process. The search of electronic health databases initially retrieved 10,621 publications. After discarding duplicates, we obtained 7,424 references which were screened by title and abstract. Eighty articles were retained for full-text screening. As part of this evaluation, we contacted the corresponding authors of 20 studies to verify whether the trialed intervention met our *a priori* definition for SDM. As a result of our evaluation, six studies were included for the final data synthesis. **TABLE 2** shows the 14 studies that were excluded from the analysis and reasons for exclusion.

2.4.2 Characteristics of included studies

TABLE 3 displays the characteristics of included studies. Six RCTs[21, 43-47] met inclusion criteria (n=1,834 participants). The publication dates ranged from 2007 to 2015. All six studies included patients who were diagnosed with a depressive disorder; only two studies included patients[45, 46] with anxiety disorders. Four of the six studies[44-47] were conducted in the United States, with one in Germany [21] and Saudi Arabia.[43] Three of the six included studies were parallel RCTs[43, 45, 46] and three were cluster RCTs[21, 44, 47] in which physician clinics, rather than participants, were randomized to the intervention group. Two studies were conducted in an inpatient hospital setting [43, 46], three studies were conducted in primary care settings[21, 44, 47], and one study[45] was conducted at a public health centre. The patient population varied considerably. Three studies [21, 44, 47] involved adults (18-64) with depression in primary care. One study[45] included only women with perinatal depression and low socioeconomic status. Another study[46] included only in-patients with moderate to severe depression in addition to comorbid cardiovascular disease.

Three of the six studies[21, 43, 47] employed interventions where SDM was explicitly defined *a priori*. Two of these[43, 47] quantitatively measured the SDM with a validated instrument such as the OPTION tool[48], and one study[21] measured SDM using a combination of the Patient Perceived Involvement in Care Scale (PICS)[49] and the patient participation scale (MSH-scale). One study[43] assessed a pharmacist intervention based on SDM that provided direct patient care compared to usual pharmacy services. The other two studies that explicitly defined SDM[21, 47] involved the use of an evidence-based decision aid for antidepressants, compared to primary care as usual with no decision aid. Three studies[44-46] consisted of collaborative care interventions in which SDM was confirmed to be incorporated into the intervention by the corresponding authors. Collaborative care was generally delivered as a multicomponent depression intervention including patient education and treatment coordination led by a patient care manager.[44-46]

2.4.3 Risk of bias within studies

The included RCTs were at moderate risk of bias. Two studies did not report random sequence generation methods[44, 47]; five studies did not report allocation concealment strategies[21, 24, 43, 44, 46, 47]; two studies[43, 47] did not blind the participants or outcome assessors, three studies did not provide a clear description[21, 44, 45]; one study[47] did not adequately blind the outcome assessor, three studies were unclear[21, 44, 46]; two studies[21, 47] suffered from incomplete reporting of outcome data, one

study did not clearly pre-specify outcomes.[44] No other sources of bias were identified. The risk of bias table (**FIGURE 2**) was made in Review Manager 5.3.

2.4.4 Risk of bias across studies

Assessment of publication bias was not conducted due to an insufficient number of included studies (less than 10) per Cochrane recommendations.[50]

2.4.5 Impact of SDM on clinically relevant outcomes

2.4.5.1 Symptoms of anxiety

Only one of the six included studies[45] reported whether SDM impacted symptoms of anxiety. Grote *et al.*[45] found that a collaborative care intervention inclusive of SDM (n=83 participants) reduced the number of participants who met the criteria for anxiety on the GAD-7 at 18-month follow-up compared to the control (MSS-Plus) condition (n=81 participants) [n=152, (intervention = 10.0% vs. control = 22.2%) OR= 0.39 (95% CI = 0.16 – 0.97)]. While there was a moderate effect size (ES) [ES= 0.52], only one study reported symptoms of anxiety, resulting in low certainty of evidence due to imprecision using the GRADE criteria.[51]

2.4.5.2 Symptoms of depression

Five of the six included studies [21, 43-45, 47] reported whether SDM impacted symptoms of depression. Grote *et al.*[45] reported that a collaborative care intervention inclusive of SDM (MOMCare) was associated with a decrease in mean depression severity on the SCL-20 compared to control (MSS-Plus) at 6-month follow-up [n=157, mean difference = -0.24 (95% CI= -0.46 – 0.03), p=0.03], and 18-month follow up [n=152, mean difference = -0.25 (95% CI= -0.45 – 0.04), p=0.02]. Four studies[21, 43, 44, 47] reported no change in depression severity compared to control conditions. Depression was measured in a variety of ways, including depression severity using the PHQ-9, SCL-20, and HADS. Given the variation in outcome results, the certainty of the evidence was rated moderate due to inconsistency.[51]

2.4.5.3 Health-related quality of life

One of six studies[43, 46] reported whether SDM impacted health-related quality of life. Aljumah *et al.*[43] reported no change in health-related quality of life due to usual pharmacy services plus pharmacist interventions based on SDM compared to usual pharmacy services after 6-month

follow-up. Health-related quality of life was measured using the EQ-5D. Given that only one included study was available for the GRADE rating and the study results were inconclusive, the certainty of the evidence on HRQL outcomes was rated low due to imprecision.[37]

2.4.5.4 Receiving evidence-based depression treatment

Three research teams[44-46] reported whether SDM impacted the receipt of adequate depression treatment. Adequate depression treatment was defined by Huffman *et al* .[46] as either (i) prescription of an antidepressant at a clinically effective dose according to treatment guidelines or (ii) referral to a mental health treatment provider for psychological therapy. This was measured using the medication possession ratio[52] and by obtaining information from patient charts. These studies[44-46] found that the collaborative care models involving SDM increased the likelihood of receiving either anti-depressant therapy or referral to psychological therapy. Chaney *et al.*[44] found that the EBQI-CCM intervention (n=268) improved the likelihood of receiving an adequate dosage of antidepressant therapy (65.7% received adequate dosage) seven months post baseline compared to the non-EBQI-CCM intervention (n=238, 43.4% received adequate dosage) [difference=22.3, $p<0.001$]. Grote *et al.*[45] reported that the "MOM-Care and MSS-plus group" (n=83) intervention group had higher rates of antidepressant use regarding group ($X^2=8.10$, df=1, $p<0.01$) and time ($X^2=18.67$, df=3, $p<0.001$) effects, compared to the Maternity Support Services (MSS-Plus) control group (n=81). The intervention group also displayed a higher adherence rate than the control group, with statistical significance ($X^2=10.0$, df=1, $p=0.002$). In addition, Huffman *et al.,* [46] found that the collaborative care intervention group (n=90) had a significantly higher likelihood of being prescribed adequate depression treatment compared to the usual care control group (n=85) (intervention: 64/89=71.9% vs. control: 8/84=9.5%; $X^2=71.5$; df=1; $p<0.001$). At 3 months, the effect size was (ES=0.66); 6 months (ES=0.52); 12 months (ES=0.54); and 18 months (ES=0.05). The certainty of the evidence was downgraded to moderate due to risk of bias among the included studies.

2.4.5.5 Patient satisfaction with care

The research teams of five of the six studies[21, 43-45, 47] discussed whether SDM impacted patient satisfaction with care. Four groups[21, 43, 45, 47] found an increase in patient satisfaction as a result of SDM interventions, while one group[44] found no statistically significant difference. Aljumah *et al.* [43] indicated that after 3 months of treatment, the group that received pharmacy services based on

SDM (n=110) had significantly higher scores on treatment satisfaction than did the group that received usual pharmacy services (n=110) (t=2.33, p=0.02). After 6 months of treatment, the effect on treatment satisfaction was still statistically significant (t=3.55, p<0.001). The measurement tool used was the TMQM. Grote *et al.*[45] found that the MOMCare group participants (n=83) reported higher mean levels of satisfaction compared to the MSS-plus group (n=81) at follow-up, with no significance in the main effect for time (X^2=0.36, df=3, p=0.95) but statistical significance for group main effect (X^2=8.28, df=1, p=0.004).

In addition, Leblanc *et al.*[47] reported that patients in the decision aid intervention group (n=158) expressed higher overall satisfaction with treatment compared with the control group (n=139), risk ratio (RR), from 1.25, (p=0.81) to RR, 2.40, (p=0.002), respectively. There was no significant effect found between groups on the questions asking whether the "Right amount of information given" (p=0.81) or "Information given was extremely clear" (p=0.09). Question items asking whether "Information was extremely helpful" (p=0.01), "Strongly desire to receive information this way for other treatment decisions" (p=0.05), and "Strongly recommend the way information was shared to others" (p=0.002) were statistically significant between groups. A 5-point Likert Scale was used for this measurement. In addition, Loh *et al.*[47] found using a t-test that patients in the patient-centred decision aid intervention group (n=128) had significantly higher satisfaction levels at the post-intervention stage compared to the control group (n=66) (p=0.014). However, since this questionnaire measurement tool was not administered at baseline, no temporal comparison of differences in satisfaction was possible. Finally, one study[44] found no statistical significance for overall patient satisfaction; Chaney *et al.*[44] stated that 62.4% of the Evidence-Based Quality Improvement Collaborative Care Model (EBQI-CCM) intervention group (n=288) reported that they were "satisfied or very satisfied with mental health care". Moreover, 67.3% of the non EBQI-CCM group (n=258) answered the survey question affirmatively as well (p=0.27).

2.4.5.6 Treatment adherence

Three of the six research teams[21, 43, 47] studied the influence of SDM on treatment adherence. In one case[43], the intervention was a provided by a pharmacist and reported a significant difference between the intervention and the control group. The authors of the other two studies reported no significant difference between treatment groups. Aljumah *et al.*[43] found that at 3-month follow-up, the intervention group (n=110) reported significantly higher scores for medication adherence

compared with the control group (n=110) (t=2.88, p=0.004). Statistically significant results were also observed at 6-month follow-up (t=4.06, p<0.001). The MMAS was used for measurement of adherence. Leblanc *et al.*[47] reported that no clinical variation was found between treatment adherence percentages for patients in the decision aid arm (n=158, 86.2%) and the control arm (n=135, 93.2%) (p=0.19). Loh *et al.*[21] found similar results, where no statistical differences in patient-reported adherence were found between the patient-centred intervention group (n=191) and the control condition participants (n=96) (p=0.73). This was also the case for physician-rated treatment adherence in the intervention and control groups (p=0.56). An investigator-developed 5-point Likert Scale was used for measurement. Due to the inconsistency in outcome definitions and measurements across the articles, the certainty of the evidence was low.

2.4.5.7 Patient involvement in health decision-making

Three of six research teams[21, 45, 47] studied whether SDM impacted patient involvement or engagement in health decision-making. Grote *et al.*[45] found that 97.5% of the participants in MOMCare intervention (n=83) and MSS-plus group (SDM) were engaged in treatment compared to 35.2% of the MSS-Plus group (n=81) [n=152, OR=72.7 (95% CI= 16.5 – 321)]. Leblanc *et al.*[47] used cluster-adjusted t-tests and found that the decision aid group (n=158) was significantly more involved in the decision-making, with 47% of the intervention group participants reporting involvement compared with 33% of the control group (n=139) (p=0.001). The OPTION tool was used in this study to measure patient involvement in decision-making. Loh *et al.*[21] stated that the intervention group (n=191) had higher patient participation in treatment from pre- to post-intervention. This was the case with the physician-rated survey scale (PICS-DF) (p=0.001) as well as the patient scale (MSH-scale) (p=0.01). Furthermore, the "group vs. measurement" effect analysis in the PICS-DF, or the interaction effects between group assignment and measurement points in the study, also indicated statistical significance (p=0.03). The authors stated that this may be evidence of the intervention improving physician reinforcement of patient participation. The control group (n=96) did not have any significant differences from pre- to post-intervention across the PICS-DF (p=0.87) and MSH-scale (p=0.26). The certainty of the evidence was low due to the inconsistency in the outcome measurement and reporting, and low number of included studies.

2.4.5.8 Consultation time

Two of the six research teams[21, 47] studied whether SDM affected consultation time. Both studies reported no change in consultation time as a result of using SDM facilitated by decision aids. Leblanc *et al.*[47] found no clinically significant differences in clinical encounter duration between the decision aid intervention group (n=158) and the control group (n=139). The mean time for the intervention group was 44 (SD=22) minutes, while the control group was 48 (SD=27) minutes (p=0.47). In addition, Loh *et al*.[21] reported that there was no statistical difference in clinical consultation time between the intervention (n=191) and control groups (n=96) for both within-group pre- and post-treatment comparisons (intervention: p=0.48), control: p=0.64), and between the treatment arms (p=0.68). The quality of the evidence obtained was low due to inconsistency in reporting outcome data, and low number of included studies.

2.4.6 Additional analyses

2.4.6.1 Emerging adults

We were unable to obtain any studies or data specifically on emerging adults.

2.4.6.2 SDM alone versus collaborative care with SDM

Three RCTs[21, 43, 47] conducted investigations of SDM interventions without the use of collaborative care, and three RCTs [44-46] conducted investigations of collaborative care interventions involving SDM. The studies involving collaborative care differed by using multiple health providers, coordinated by a care manager to evaluate and coordinate the personalized care of individuals with depression based upon unique needs.[44-46] Studies of SDM alone[21, 43, 47], primarily involved interactions between one health care provider and the patient.

All three RCTs [44-46] using collaborative care models found that patients with depression were more likely to receive adequate depression treatment compared to usual care without SDM, with statistical significance [Chaney *et al*., 2011[44]: p=0.001; Grote *et al*., 2015[45]: p=0.01; Huffman *et al.* 2011[46]: $p < 0.001$]; however, the studies of SDM without collaborative care did not report this outcome. All three research groups who studied SDM[21, 43, 47] found that SDM improved satisfaction with care, and one of the two groups who studied collaborative care[45] reported that SDM improved satisfaction with care. Comparisons of other clinically relevant outcomes could not be conducted due to inconsistency in reporting.

2.4.6.3 SDM facilitated by using a decision aid

Two research teams used decision aids to facilitate SDM, compared to control groups that did not use decision aids.[21, 47] No change was found in depressive symptoms or treatment adherence in either study. One research team who studied decision aids reported an increase in patient knowledge[47]; both research groups who studied SDM and decision aids reported improvements in satisfaction with care. However, two of the three teams who studied SDM without decision aids[43, 45] also reported improved satisfaction with care. Both research teams who studied SDM with decision aids found patient participation improved, but the only team studying SDM without decision aids[45] also found patient participation improved as a result of collaborative care. Both teams that studied SDM studies with decision aids reported no change in consultation time. Comparisons to studies without decision aids were not possible due to limitations in outcome reporting.

2.5 DISCUSSION

To our knowledge, this is the first systematic review to examine whether SDM impacts clinically relevant outcomes in adults diagnosed with anxiety and depressive disorders. We found preliminary evidence that the use of SDM may favourably impact outcomes such as satisfaction with care and patient involvement in decision-making. We found evidence that SDM, when used in conjunction with a collaborative care intervention, likely improves the likelihood of receiving adequate depression treatment, and preliminary evidence that SDM may facilitate a reduction in symptoms of anxiety. However, only one study reported anxiety as an outcome, and a statistically significant difference was only detected at 18-month follow-up.[45] It appears unlikely that SDM by itself improves symptoms of depression, as only one of the five studies that measured symptoms this outcome demonstrated a statistically significant improvement. The lone study[45] that demonstrated an improvement also used collaborative care in addition to SDM, which may be partially responsible for the observed effect.

Among the included studies, one study suggested collaborative care involving SDM may improve symptoms of anxiety or depression.[45] SDM and collaborative care studies appeared to show promising results on improving outcomes such as patient satisfaction with care, but the SDM and collaborative care studies largely measured different outcomes. Over the past twenty years, a

considerable evidence base has grown in support of collaborative care for improving outcomes in patients with anxiety and depression. For example, several large systematic reviews and meta-analyses have shown that collaborative care is more effective than usual care in improving both quality of care outcomes and symptoms of anxiety and depression for short and long-term.[38, 39, 53] Therefore, we hypothesize that it is possible that collaborative care may either facilitate or enhance the impact of SDM.

The literature suggests that decision aids may facilitate SDM [29, 54], but it was unclear from our data whether decision aids impacted the effectiveness of SDM in our target population. We were only able to compare the impact of SDM via the use of a decision aid on two outcomes (satisfaction with care and patient participation), and both approaches were effective. More research is needed to clarify the impact of decision aids on the effectiveness of SDM in people with anxiety and depressive disorders. Additionally, no relevant studies were found in the emerging adult population, and the corresponding authors of the included studies were not able to provide any additional data to conduct any further analysis. More research is needed to explore the potential impact of SDM in emerging adults as there is evidence that emerging adults may avoid mental health services and may benefit from approaches that facilitate increased engagement.[36, 55-58]

The findings of our systematic review are consistent with previous systematic reviews on SDM in mental health conditions. We also found that SDM primarily improved satisfaction with care and patient involvement in decision-making.[20, 23, 24] Our review builds on the work of Samalin *et al.,* (2018) by including studies of anxiety disorders and exploring additional analyses around emerging adults, and decision aids.[23]

2.5.1 Limitations of the included studies

The included studies were at moderate risk of bias, which weakened the certainty of the evidence. The primary issues were around concealment of allocation and inconsistently defined and measured SDM interventions. Moreover, to the best of our knowledge, there is no universally accepted definition of SDM in the literature. The lack of a consistently defined construct of SDM in the literature poses challenges for researchers to assess the occurrence and effectiveness of SDM across multiple studies.[59]

Only two of six studies measured SDM using a validated instrument such as the OPTION scale[60], therefore it was difficult to assess to what extent SDM was delivered, and whether SDM was present in the control groups. While the three collaborative care studies involving SDM[44-46] measured adequate depression treatment (i.e., prescribed an antidepressant based on clinical practice guidelines or referred to psychological therapy) as a primary outcome, none of the other SDM studies measured this outcome. Our observation is supported by a recent scoping review[61] which also found inconsistencies among SDM outcomes and tools, which may ultimately reflect heterogeneity in how SDM is defined and measured. Validated and consistent outcome reporting in future clinical trials on SDM is needed to further synthesize the results required to better inform policy and clinical practice.

Some evidence shows that SDM is beneficial when used over time with a health care provider and may not always occur on the initial visit.[47] A majority of the included studies only used SDM during a single clinic visit, which may underestimate the potential impact of SDM when used in a series of clinical encounters over time.

2.5.2 Strengths and limitations of the review

Our study has several strengths. We performed a comprehensive search spanning five health databases using literature-informed search terms related to SDM, anxiety, and depressive disorders. A unique aspect of this study was that we operationally defined SDM and created rigorous inclusion criteria based on this definition. Furthermore, we contacted authors of studies where it was unclear based upon the reporting of whether SDM occurred. Two independent reviewers performed all stages of screening and analysis. Additionally, this systematic review included several clinically relevant outcomes that may be useful for informing clinical practice and policy.

There are also several limitations of this review that may impact the interpretation of findings. SDM is sometimes studied in other study types such as observational or qualitative studies, and the exclusion of these study types may not provide a clear map of all evidence investigating SDM in adults with anxiety and depression. However, including studies with these methods would have increased methodological heterogeneity in the review, and would not have helped address our review objectives. Due to feasibility concerns, we did not search for literature outside of English-language, which may have limited the inclusion of potentially relevant studies. This limitation may

weaken the generalizability of this review. Since the objective of this review was on SDM, we did not design a search strategy around collaborative care. We acknowledge that collaborative care may sometimes involve SDM, and therefore these studies may have been missed in our search.

Clinical heterogeneity across the included studies posed challenges for data synthesis and the interpretation of the results. For example, three of the studies involved patients with depression from primary care settings, while the other three studies involve specific populations such as inpatients with cardiovascular disease, women with perinatal depression, and psychiatric inpatients receiving care from pharmacists. Moreover, each of these studies delivered SDM in a unique way, which made making comparisons difficult and combining results via meta-analysis not possible.

For example, three of the six studies[44-46] used a collaborative care intervention in addition to SDM. Notably, the collaborative care approach in these studies involved multiple modalities in addition to SDM, which may have increased the likelihood of observing a significant effect. Furthermore, meta-analysis was also not possible due to inconsistency in outcome reporting and heterogeneity in both the measurement of the independent variable (e.g., SDM) and the outcome measurements. Additionally, due to the low number of included studies, we were not able to assess publication bias, which cannot be entirely dismissed.

2.5.3 Conclusion

Overall, the evidence we obtained suggests that SDM may provide some benefits in the treatment of adults with anxiety and depressive disorders, with little to no evidence of harm. The low number of studies and high clinical heterogeneity among the included studies prevented us from drawing robust conclusions; however, our findings are consistent with previous systematic reviews on SDM in patients with other mental health conditions. More high-quality research using a consistent definition (and reliable measurements) of SDM is needed to advance knowledge in the field. Furthermore, we suggest additional research in emerging adults, who may especially benefit from the use of SDM when making decisions about mental healthcare.

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2.7 ADDITIONAL INFORMATION

2.7.1 Declaration of interest

None.

2.7.2 Funding

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2.7.4 Author contributions

All authors have made significant intellectual contribution to the development of this manuscript. TM and SV developed the research questions and methods. TM produced the first draft of the manuscript. CS, KO, AA, RL, XL assisted in refinement of the research questions and revisions of the manuscript. TM and a health research librarian with systematic review expertise designed the search strategy and performed the database searches. TM and CS screened, extracted and analyzed the data. SV has expertise in systematic reviews and provided detailed feedback on all manuscript drafts. All authors have contributed substantially to the conception, acquisition, analysis, interpretation of data, and have approved the final version of this manuscript.

2.7.5 Data availability

The data that support the findings of this study are available from the corresponding author, SV, upon reasonable request.

2.8 TABLES

TABLE 1. Inclusion/exclusion criteria

	Included	**Excluded**
Population	• Adults 18+ . • Primary diagnosis of any anxiety or depressive disorder (DSM-III criteria or later). • Other mental health comorbidities (e.g., substance use disorders). • Physical health comorbidities (e.g., diabetes, cardiovascular disease). • Inpatients or outpatients.	• Studies with mean age over 64 years. • Diagnosis of schizophrenia. • Diagnosis of bipolar disorder. • Patients mandated to treatment. • Patients at risk to harm self or others (e.g., suicidal ideation).
Intervention	• SDM according to the Elwyn *et al.*[29] criteria.	• Studies where the use of SDM was not clear.
Control	• Any.	• Studies where SDM was present in both treatment and control arms • Uncontrolled studies.
Outcomes	• Any clinically relevant patient outcome.	• Health care provider outcomes.
Study type	• Randomized or non-randomized prospective controlled trials.	• Systematic reviews. • Observational studies. • Qualitative studies. • Case reports. • Expert opinion articles.

		• Grey literature.

TABLE 2. Studies excluded due to intervention not meeting SDM criteria

Author	Article Name	Contact author successful?	Author's reply
Alexopoulos *et al.* 2013	Personalised intervention for people with depression and severe COPD	Yes	Study does not meet SDM criteria.
Aragones *et al.* 2009	Implementing collaborative care for depression treatment in primary care: a cluster randomized evaluation of a quality improvement practice redesign	No	
Dobscha *et al.* 2006	Depression Decision Support in Primary Care: A Cluster Randomized Trial	Yes	Study does not meet SDM criteria.
Dunlop *et al.* 2012	Depression beliefs, treatment preference, and outcomes in a randomized trial for major depressive disorder	Yes	Study does not meet SDM criteria.
Dwight-Johnson *et al.* 2010	Effectiveness of collaborative care in addressing depression treatment preferences among low-income Latinos	No	
Eli *et al.* 2008	Randomized controlled trial of collaborative care management of depression among low-income patients with cancer	No	
Eli *et al.* 2011	One-year postcollaborative depression care trial outcomes among predominantly Hispanic diabetes safety net patients	No	

Katon *et al.* 2015	A randomized trial of collaborative depression care in obstetrics and gynecology clinics: socioeconomic disadvantage and treatment response	No	
Kravitz *et al.* 2013	Patient engagement programs for recognition and initial treatment of depression in primary care: a randomized trial	Yes	Study does not meet SDM criteria.
Lin *et al.* 2005	The influence of patient preference on depression treatment in primary care	No	Study does not meet SDM criteria.
Melville *et al.* 2014	Improving care for depression in obstetrics and gynecology: a randomized controlled trial	No	Study does not meet SDM criteria.
Pyne *et al.* 2010	Cost-effectiveness analysis of a rural telemedicine collaborative care intervention for depression	No	Study does not meet SDM criteria.
Sharpe *et al.* 2014	Integrated collaborative care for comorbid major depression in patients with cancer (SMaRT Oncology-2): a multicentre randomised controlled effectiveness trial	Yes	Study does not meet SDM criteria.
Stewart *et al.* 2014	Effect of collaborative care for depression on risk of cardiovascular events: data from the IMPACT randomized controlled trial	No	
Vergouwen *et al.* 2009	Improving patients' beliefs about antidepressants in primary care: a cluster-randomized controlled trial of the effect of a depression care program	No	

Vigod *et al.* 2019	A patient decision aid for antidepressant use in pregnancy: Pilot randomized controlled trial	Yes	Study does not meet SDM criteria.

TABLE 3. Characteristics of included studies

Study, year (country)	Study design	Inclusion criteria	Sample size	Duration of study	Setting	Age range, mean age (SD), (%) male	Description of intervention (n participants)	Description of control conditions (n participants)	Outcomes	Outcome measurement instruments	Data collection intervals
Aljumah *et al.* 2015 [43] (Saudi Arabia)	Parallel RCT	Major depressive disorder (DSM-IV), no history of psychosis or bipolar disorders, no drug or dependency history, no cognitive impairment.	n=239 patients	11 months	Inpatient	18-60 years, NR, 41% male	Shared decision making facilitated by pharmacist intervention focused on enhancing patients' involvement in decision making by assessing their beliefs and knowledge about	Usual pharmacy services (n=120)	-Medication adherence -Patient's beliefs about medicine -Depression severity -Patient involvement in decision-making -Health-related quality of life -Patient	-MMAS (mean scores) -BMQ (Specific and General versions, mean scores) -MADRS (mean scores) -OPTION (overall scores*)	Baseline, 3 month follow up, 6 month follow up

							antidepressants. (n=119)		satisfaction with treatment	-EQ-5D (mean scores) -TSQM 1.4 (mean scores)	
Chaney *et al.* 2011[44] (USA)	Cluster RCT	Major depressive disorder (PHQ-9 ≥ 10), no acute suicidality	n=546 patients	21 months	Primary care	Mean 64.0 intervention – 64.4 years control, 95.8% male intervention, 96.5% male control	EBQI applied to collaborative care model implementation. (n=288)	Usual care: Non-collaborative care model (n=258)	-Receipt of appropriate treatment -Depression severity -Patients below threshold for major depression -Physical functional status	Antidepressant fill at appropriate dosage in the seven-month time period, and the medication possession ratio (MPR) -PHQ-9 (mean scores) -PHQ-9 (%< 10)	Baseline, 7-month follow up

									-Emotional functional status -Satisfaction with mental health care	-SF-12 (mean role physical scores) -SF-12 (mean role emotional scores) -% somewhat or very satisfied	
Grote *et al.* 2015 [45](USA)	Parallel RCT	18 years, diagnosis of probable major depressive disorder or diagnosis of probable dysthymia	n=168 patients	49 months	Public health centers	18-44 years, 27.4 (6.1), 0% male	"MOMCare,"a collaborative care intervention, providing a choice of brief interpersonal psychotherapy and/or antidepressant therapy (n=83)	Usual care: Maternity Support Services (n=85)	-Depression severity -Functional impairment -Treatment response -Complete remission of depressive symptoms -PSTD severity	-SCL-20 (mean scores) -WSAS (main effects) -SCL-20 (≥50% reduction from baseline score) -SCL-20 (score <0.5)	Baseline, 3, 6, 12, 18 month follow up assessments

									-Probability of GAD diagnosis -Quality of mental health care (# of sessions, antidepressant use, satisfaction with care)	PCL-C (main effects)-PHQ (overall score) -standardized questions & antidepressive use	
Huffman *et al.* 2011 [46](USA)	Parallel RCT	Acute cardiac disease, Depression (PHQ-9 ≥ 10) and 5 or more symptoms including depressed mood or anhedonia	n=175 patients	28 months	Inpatients	62.3 (12.5), 51.4 % male	Collaborative care: the care manager performed a multi-component depression intervention in the hospital that included patient education and treatment	Usual care: inpatient providers were informed of the depression diagnosis. (n=85)	-Adequate depression treatment by discharge	(1) discharge prescription of an antidepressant at a clinically effective dose based on manufacturers' package labeling and treatment	Baseline, 6-month follow up

							coordination (n=90)			guidelines for the treatment of depression or (2) referral to a mental health treatment provider for psychotherapy	
LeBlanc *et al.* 2015 [47](USA)	Cluster RCT	Moderate to severe depression and a Patient Health Questionnaire (PHQ-9) score of 10 or higher, no bipolar disorder, an appointment with a member of	n=301 patients, n=30 clinicians	24 months	Primary care	>18 years, 44 (15), 33% male	Shared decision making facilitated by physician use of a decision aid during selection of antidepressants. (n=158)	Usual care (n=139)	-Decisional conflict -Patient knowledge & satisfaction -Patient involvement in decision making -Depression (symptoms;	-DCS (overall mean scores) -Post-encounter questionnaire -OPTION (scoring recorded encounters) -PHQ-9 (mean scores; scores	Baseline, 3-month, 6-month follow up

		their primary care team, and no major barriers to providing informed consent.							remission; responsiveness) -Primary medication adherence -Secondary medication adherence -Encounter duration -Satisfaction	<5; >50% improvement) -Percent filled prescription -Proportion of days covered > 80% -Mean minutes -Investigator developed 5 point Likert scale	
Loh *et al.* 2007 [21](Germany)	Cluster RCT	Diagnosis of depression (PHQ-9), no psychotic symptoms, functional language and literacy abilities	n=405 patients, n=117 clinicians	27 months	Primary care	40.8 (13.2) - 50.4 (16.3) years, 22.2 - 34.7% male	Shared decision making facilitated by used of a decision aid during selection of antidepressants (n=263)	Usual care (n=142)	-Patient involvement -Depression severity and clinical outcome -Treatment adherence -Patient	-PICS & MSH-scale (pre-post intervention) -Brief PHQ-D (% reduction in severity) -Investigator developed 5-	-Baseline, 6-8 week follow up

									satisfaction -Consultation time	point Likert scale (patient and physician) -CSQ-8 -Minutes (documented by physician)	

Footnotes: Abbreviations: BMQ: Patients' Beliefs about Medicine Questionnaire (Specific and General versions); CSQ-8: Client Satisfaction Questionnaire; DCS Decisional Conflict Scale; EBQI: Evidence-Based Quality Improvement; HADS-A: Hospital Anxiety and Depression Scale-Anxiety Subscale; MADRS: Montgomery–Åsberg Depression Rating Scale; MMAS: Morisky Medication Adherence Scale; MSH: Man-Son-Hing-instrument; OPTION: Observing Patient Involvement in Decision-Making scale; PCL-C: Post-Traumatic Stress Disorder Checklist-Civilian Version, PHQ: Patient Health Questionnaire; PICS: Patient's Perceived Involvement in Care Scale; SCL-20: Hopkins Symptom Checklist; SF-12: Medical Outcomes Study Short Form; TSQM 1.4: Treatment Satisfaction Questionnaire for Medication, WISE: Women and Ischemia Syndrome Evaluation study; WSAS: Work and Social Adjustment Scale.

TABLE 4. Summary of the impact of SDM on clinically relevant outcomes

	Anxiety symptoms	Depressive symptoms	Quality of Life	Treatment adherence	Adequate depression treatment	Patient knowledge	Patient Satisfaction	Involvement in decision-making
N of reporting studies	1	5	1	3	3	1	5	3
Increased (p <0.05)	0	0	0	1	3	1	4	3
Decreased (p <0.05)	1	1	0	0	0	0	0	0
No change (n.s.)	0	4	1	2	0	0	1	0
Quality of evidence GRADE	Low	Moderate	Low	Low	Moderate	Low	Moderate	Moderate

Reasons for down grade	Indirectness Imprecision	Inconsistency	Imprecision	Inconsistency	Risk of bias	Imprecision	Inconsistency	Imprecision

2.9 FIGURES

2.9.1 FIGURE 1. PRISMA-Flow diagram

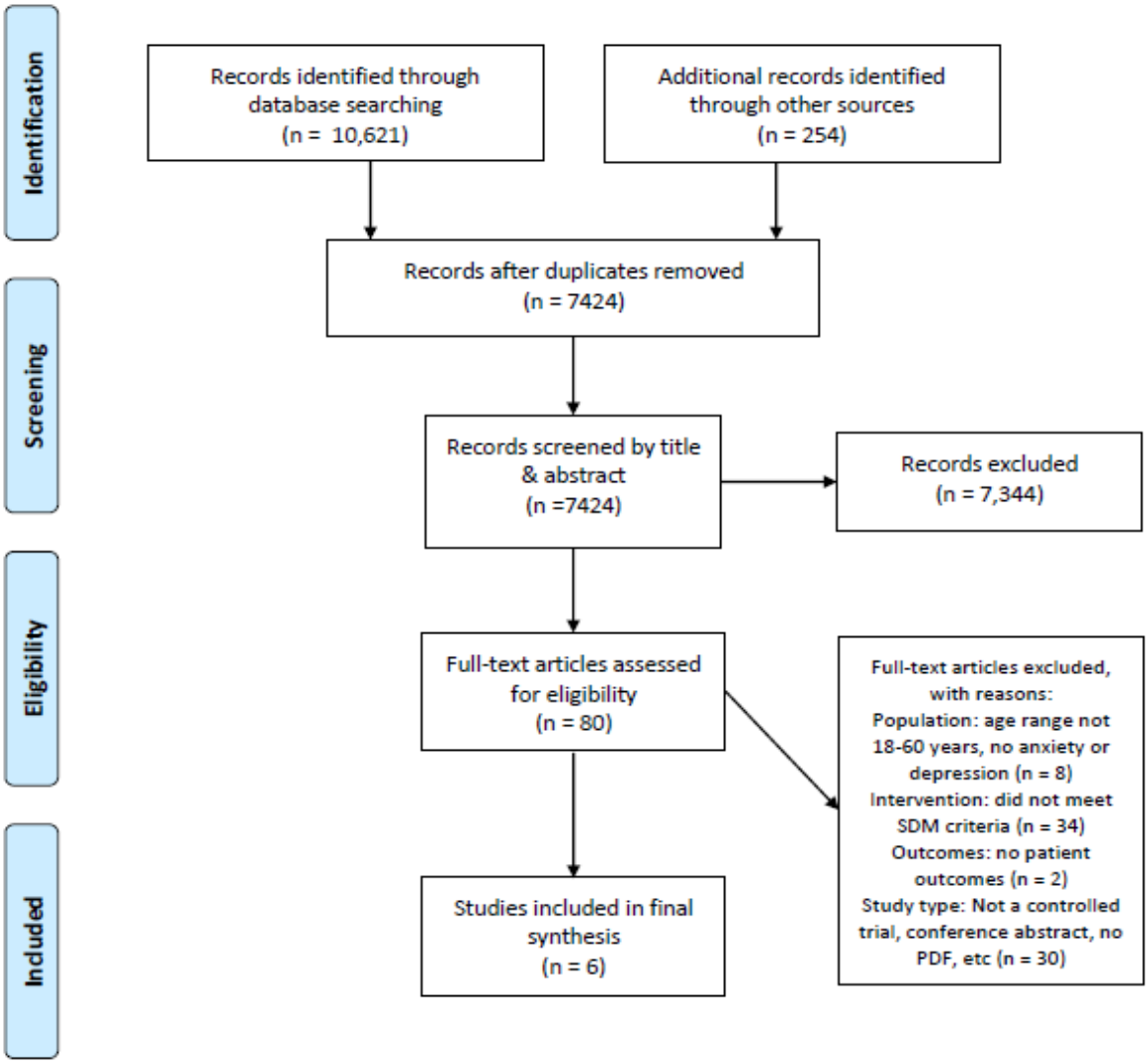
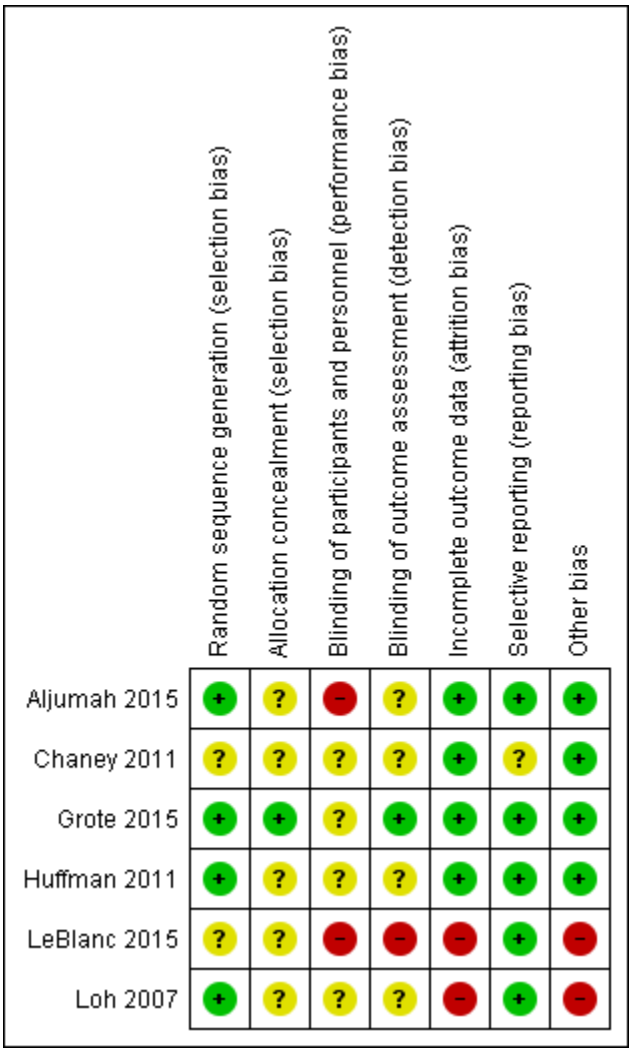


FIGURE 2. Risk of Bias (ROB) Summary of Results



Legend: Green = Low ROB; Red = High ROB; Yellow = Unclear ROB

2.10 SUPPLEMENTARY INFORMATION

SUPPLEMENARY 1. MEDLINE Search Strategy

1. *Decision Making/
2. Shared decision making.ti,ab.
3. decision support.ti,ab.
4. patient participation.ti,ab.
5. Patient Participation/
6. patient involvement.ti,ab.
7. *Patient Preference/
8. patient preference.ti,ab.
9. patient engagement.ti,ab.
10. patient perspective.ti,ab.
11. or/1-10
12. exp Depression/
13. exp Depressive Disorder/
14. Dysthymic Disorder/
15. depression.ti,ab.
16. exp Anxiety/
17. exp Anxiety Disorders/
18. (anxiety or phobia or phobic or panic).ti,ab.
19. or/12-18
20. 11 and 19
21. limit 20 to humans
22. limit 21 to english language

SUPPLEMENTARY 2. Deviations from protocol

We also excluded studies of older individuals (mean age: 65+ years) as the treatment preferences and experience of anxiety and depressive disorders in older adults may not be comparable to younger populations.[62,]

CHAPTER 3: The lived experience and decision-making preferences of emerging adults in the treatment of anxiety and/or depression: a qualitative exploration

Authors

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This manuscript has been submitted to a peer-reviewed journal

3.1 ABSTRACT

A narrative inquiry was conducted exploring the life stories and mental health decision-making preferences of twelve emerging adults in treatment for anxiety and/or depression in Alberta, Canada. Data were collected from two outpatient, one primary care, and one inpatient mental health facilities. Unstructured in-depth interviews were audio-recorded and transcribed verbatim. Reviewer reflections and extensive summaries were written to construct the narratives. Common narratives included: experiencing childhood stress, high social pressures during adolescence, desire for social withdrawal, and self-medicating with substances and/or alcohol as a coping strategy. Professional mental health services were often only considered as a last resort. Receiving positive social support from trusted individuals such as close friends or family members may facilitate seeking timely care. Participants appeared to value involvement in health-related decision-making. More qualitative research is encouraged to inform person-centred research and service development.

Keywords

Anxiety, depressive disorders, qualitative, adolescence, patient engagement.

3.2 INTRODUCTION

Emerging adults are characterized as individuals undergoing the transition from adolescence to young adulthood, occurring roughly between the ages of 18-25 years.[1, 2] From a psychosocial perspective, Arnett (2004, 2005) described emerging adulthood as a developmental period associated with i) identity exploration and decreased parental attachment, ii) social experimentation, iii) "feeling in-between", iv) ontological/self-development, and v) socioeconomic instability.[3, 4] Emerging adults are commonly exposed to novel environmental stressors including increased academic, occupational, and financial demands which may lead to symptoms of anxiety and depression.[5, 6]

Symptoms of anxiety and depression commonly interfere with coping skills required during the transition to adulthood.[7] For instance, these symptoms may decrease executive functioning in university students leading to impaired academic performance.[8, 9] Anxiety and depressive disorders may emerge when symptoms are not identified and/or treated early[10], and commonly onset during emerging adulthood.[11, 12] These disorders are associated with the onset of several chronic conditions, such as obesity[13, 14], type 2 diabetes[15], and substance use disorders.[16] Emerging adults are the least likely to obtain professional mental health care of any adult age group, and only one-third of symptomatic individuals receive professional services.[17] Previous systematic reviews suggest emerging adults are more likely to prefer self-reliance, and self-medicate with substances and/or alcohol.[17] Other qualitative studies suggest emerging adults with depression commonly report experiencing and internalizing shame and/or stigma when addressing mental health concerns[17, 18], which may underpin unsatisfactory treatment utilization.

Improving mental health care in young people has been recommended by experts as a global priority.[19, 20] Scholars argue that when mental health services are tailored to the needs of vulnerable populations (e.g., emerging adults), health outcomes may improve.[21] Moreover, a deeper understanding of the lived experience of vulnerable populations may increase compassion and empathy[22, 23], and decrease implicit biases among clinicians, which may inadvertently influence clinical decision-making.[24, 25] Moreover, utilization of lived experience data may inform clinical practice and services design aimed to decrease stigma and health disparities in mental healthcare, while facilitating early identification and treatment of mental health disorders.[19, 20, 26, 27]

3.2.1 Objective

The objective of this study was to explore the life stories of emerging adults who sought treatment for anxiety and/or depression and explore how these individuals prefer to make mental health-related decisions.

3.3 METHODS

3.3.1 Qualitative approach and research paradigm

A qualitative study was conducted guided by the principles of narrative inquiry.[28] Narrative inquiry is a qualitative method which aims to produce rich and descriptive accounts of individual's lived experiences in the form of storytelling.[29] Narrative inquiry follows an inductive approach based on a constructivist epistemological framework, using a variety of data collection methods, including: in-depth and unstructured verbal interviews, field notes, and interviewer self-reflection exercises to construct a narrative account of individual's experience.[28] The Standards of Reporting Qualitative Research (SPQR) statement[30] was consulted to guide reporting of the results.

3.3.2 Researcher characteristics and reflexivity

The research team for this study included a PhD student with a background in public health and neuroscience, three physicians, and one nurse. The second author was the lead psychiatrist at two of the participating clinics. The third author is a physician and researcher in primary care. The fourth author is a psychiatrist and neuroscience researcher, the fifth author is a pediatrician and clinical researcher, and the senior author is a registered nurse and qualitative researcher. The lead author also took part in a summer student internship at mental health and primary care settings in Red Deer, Alberta, which included an opportunity to observe all aspects of the clinic's work, obtain organizational documents, and shadow licensed health care staff. The first author took part in a separate clinical observership in one outpatient and one inpatient psychiatric setting in Edmonton, Alberta, in addition to volunteering at a harm reduction service in each city. All participants were interviewed by the first author, who had previous experience interviewing individuals receiving mental health care, but no prior relationship with any of the interviewees. The first author wrote field notes before and after data collection and during his clinical observations.

3.3.3 Context and setting

The study was conducted during the spring and summer of 2019 in Alberta, Canada, during a major drug overdose crisis, but prior to the onset of the COVID-19 pandemic. Alberta is a geographically large province in western Canada of 4.37 million residents with a single-payer health care system. Participants were recruited from one large inpatient mental health centre, one young adult outpatient mental health centre, and one primary care centre in Edmonton, Alberta. Edmonton is a large metropolitan city in Western Canada of approximately 1.3 million residents. Participants were also recruited from one outpatient addiction and mental health centre in Red Deer, Alberta. Red Deer is a predominantly rural community of approximately 104,000 residents. The mental health services received by the included participants prior to data collection were covered financially by the provincial health system.

3.3.4 Sampling strategy

Managers of several primary care, outpatient addiction and mental health clinics, and harm reduction centres in Alberta were contacted via email to obtain initial interest/availability. After ethics approval and informed consent was obtained from the clinic management, licensed healthcare providers were recruited on a voluntary basis to assist with screening participants for eligibility. A small card identifying inclusion/exclusion criteria was given to health care providers to assist with screening for eligibility. The first author then met with the individuals identified by health care providers, explained the study, answered any questions, and obtained written consent from those willing to take part. Due to an absence of research funding at the time of recruitment, we were not able to provide any compensation to individuals for participation.

3.3.4.1 Participant eligibility criteria

Participant inclusion criteria: (i) individuals 18-25 years at the time of consent, (ii) current and/or past symptoms of anxiety/depression, (ii) voluntarily sought and received mental healthcare at a mental health or primary care facility in Alberta, (iii) able to provide written informed consent without a proxy, and (iv) able to understand, speak and read English.

Participant exclusion criteria: (i) individuals who are currently at risk of harming themselves or others, (ii) mandated to treatment for any reason (e.g., by the justice system), (iii) at risk of psychological harm from participating in a verbal interview (e.g., recent exposure to trauma or

severe post-traumatic stress disorder), or (iv) unable to provide informed consent for any other reason, such as intellectual disability).

3.3.5 Data collection methods

After informed consent, participants completed a sociodemographic questionnaire and the Hospital Anxiety and Depression Scale (HADS), used to describe the sample based on the presence of clinically significant symptoms of anxiety and/or depression. The HADS is split into two sections (HADS-Anxiety and HADS-Depression). Clinically significant symptoms of anxiety were defined as scores of ≥8 on the HADS-A; clinically significant symptoms of depression were defined as scores of ≥8 on the HADS-D. A systematic review suggests that these cut points have a high positive predictive value for identifying individuals with a variety of anxiety and/or depressive disorders.[31]

3.3.5.1 Interview process

After sociodemographic data was obtained, unstructured verbal interviews were conducted with each participant. Open-ended questions such as "please describe what your daily life is like" were used to initiate the inquiry. Probing (i.e., facilitation) questions about participants, early childhood years, adolescent years, description of an individual's interpretation of the meaning of "recovery" and "relapse", in addition to preliminary queries around values and preferences for making health decisions. Interviews were conducted in a private office space at each clinic site, with only the interviewer and the participant present. All participants underwent a short debriefing (approximately 5-10 minutes) prior to departure for precautionary reasons. The Alberta crisis hotline number (403-266-4357 (HELP)) was provided on the participant's copy of the consent form, which also included the healthcare provider's contact information and the phone number for the health research office at the University of Alberta.

3.3.6 Data analysis

The interview transcripts were analyzed using NVivo 12 (QSR International). The interview, audio, clinical field notes, and each transcript were read by the first author in a preliminary exercise. The researcher then wrote detailed summaries about the key moments expressed in each participant's transcript, ranging from early childhood to the emerging adulthood years. The

summaries and field notes were reviewed in collaboration with the senior author to identify any key patterns or narratives in the data. Several iterations of the analysis were performed to ensure key details were inadvertently omitted.

3.3.6.1 Techniques to enhance trustworthiness

Multiple established approaches were used to ensure verification and trustworthiness of the data.[32, 33] Methodological coherence was obtained by selecting a study design that appropriately followed the research question. Additionally, only one participant was interviewed per day, thus allowing the first author to engage in critical reflection activities (e.g., journaling) to become aware of any potential personal biases that may impact the results. The first author made note of these, discussed these with the senior author, and accounted for these in the data analysis. In addition, the first author completed graduate level coursework, obtained professional training for conducting interviews and performing data analysis, and had previous experience conducting interviews on a related study. The first author was diligent about refraining from making comments and/or judgments about the participants' stories or narratives during the interview process. The interviews transcripts were reviewed by the senior author, who has expert-level experience in qualitative research to enhance intercoder reliability.[34]

3.3.7 Confidentiality and storage of data

Interviews were conducted in a private office space at each clinic site, with only the interviewer and the participant present. Data were recorded by the first author on a digital voice recorder, and then transcribed verbatim and uploaded to the Health Research Data Repository at the University of Alberta. All interviews were then cleaned, and personal identifiers were removed. Access to the data was strictly limited to the research team. Participants were aware and consented to have their anonymized quotes used in any resulting publication or presentation.

3.3.8 Ethics

This study was approved by the University of Alberta Health Research Ethics Board (PRO00086228).

3.4 RESULTS

3.4.1 Descriptive data

Twelve individuals were included in the study, including five from inpatient and six outpatient mental healthcare settings. Five were male, and six individuals were of Caucasian descent. None of the participants were married, and six participants reported a total household income of under $20,000 per year. Eleven reported having a high school degree or equivalent. Eleven also reported having a diagnosed mental health condition. Ten individuals reported being prescribed psychiatric medication. Seven participants reported using psychoactive substances or alcohol to cope with mental health symptoms. Nine participants met HADS criteria for clinically significant symptoms of anxiety, seven met criteria for depression, and seven met criteria for both anxiety and depression. **TABLE 1** displays the descriptive data.

3.4.1.1 Qualitative descriptions

Generally, participants described diverse past childhood and adolescent experiences and family life. Some individuals identified themselves as "high achievers" who reported experiencing pressure to succeed academically, while others experienced trauma (e.g., homicide, sudden death of family member, abuse). Some experienced disruptive events in their families (e.g., divorce, interpersonal conflict), while others experienced more stable home lives. Participants commonly felt overwhelmed at some point during adolescence or during transitioning to emerging adulthood with either their occupation, academics or trying to gain social approval from friends. Once emerging, adults felt overwhelmed, many socially withdrew, and began to describe feeling isolated. A majority of the participants described using drugs (e.g., cannabis) and alcohol to cope with distress. Some participants described experiencing a variety of other mental health symptoms in addition to anxiety and depression, including panic attacks, psychotic episodes, impulsivity, aggression, dissociation, etc.

3.4.2 Narratives identified

Feeling overwhelmed

Participants often described feeling overwhelmed at some point during adolescence or emerging adult years prior to treatment admission. One participant described feeling overwhelmed immediately after graduation.

"Right after I graduated, it was just kind of overwhelming to me. I got yelled at on my first day. Like, it was my first real job and it just like kind of freaked me out, I guess."

Obtaining social acceptance/approval

Participants commonly discussed that trying to gain social approval was a stressor, particularly during adolescence or high-school years. Using cannabis was often seen as a means to gain approval from peers. The pressure from peers often increased as people became older, and participants often became self-conscious about this. One participant described smoking cannabis "every day" during his first year of high school in an attempt to gain social approval.

"My first year in high school unfortunately like, I started like smoking weed, and kind of like fell out, not into a bad crowd, but like I don't know, but just started smoking weed like every day, it was the cool thing to kind of do."

Withdrawing socially

Once symptoms of anxiety began, participants described commonly withdrawing from social or occupational settings, including feeling little desire to interact with peers or work. One participant described a lack of interest in socializing with friends.

"Recently, in school I always had a big group of friends… grew up together, but out of school I haven't really seen anybody. I don't go out very often."

Coping with substances and/or alcohol

Participants commonly discussed feeling being more comfortable alone, and discussed shame, embarrassment when people knew they were not feeling well. They also commonly discussed using alcohol or cannabis – often alone – to cope with acute stress or adversity. One individual expressed strong dismay at being "felt sorry for" and would rather drink alcohol by himself.

I think I felt more comfortable being alone with my misery. However, I didn't like, I hated feeling like one of those people that everyone felt sorry for. So, I'd rather, drink my sorrys away in my basement by myself, than do it at my friend's house, while they're like "it's okay."

Conflict during childhood

Participants commonly described complex interfamily dynamics and described growing up with substantial feelings of interpersonal conflict during childhood years. One individual described growing in an environment with high interfamilial conflict.

> *"Because I can only remember like a couple of really bad times with my family, and I remember mostly good times and stuff, but my mother and father like, it was constant like fighting in my house. They, I don't know what it way, but just like we hated each other, everyone hated each other and for no reason."*

Barriers to seeking care

Participants described several barriers to seeking professional mental health care, including feelings of resentment with family members, finding affordable care, anxiety, shame, stigma, and low mental health literacy.

> *"My whole youth I avoided it [mental health care]…like the plague. And when I turned 18, I just had had enough. I was like…fine. I'll see what it's going to do. I just couldn't cope anymore."*

Facilitators for seeking care

Participants described that support from someone close, such as a family member, counselor, or friend, often encouraged them to seek professional mental health care. One participant described familial conflict as both a source of distress and a support for successful treatment entry.

> *"The support from my parents really helps, and they kind of talked me into coming here and trying to get help, so…"*

If individuals did not have social support, they would often report having to "hit rock bottom" or a critically low point to consider seeking professional treatment.

> *"I think I have just, I have hit a point where I realize that doing it myself isn't going to help, going to work, so…"*

Recovery and relapse

The meaning and definition of "recovery" varied substantially among individuals. Several individuals saw that recovery meant that they could return to work or school. In the context of substance or alcohol use, many individuals desire to drink alcohol and/or use cannabis in moderation or in a more positive way, such as at a family wedding. One individual expressed interest in becoming more financially stable.

> *"Mostly just being able to take care of my own without digging a hole. Like I just want to be financially stable, while being able to use these substances but not like abusing it like more of a recreational thing."*

Another individual expressed that being able to work again may help facilitate his recovery.

> *"Just working again. Work is like one of my big things, like you know like, I worked at that liquor store for two years, and no problems really"*

The identification and meaning of symptom relapse varied substantially among individuals. Some participants defined relapse as when they notice they become less interested in their academic performance, others notice a change in their sleep, while some notice themselves beginning to withdrawal socially. One individual explained that she would notice a drop in her grades when her symptoms of depression were returning.

> *"I find that I'm…with school …I know that it's getting worse when I stop caring about my grades. Cuz, I like to maintain a B+ average, is what I've been trying to hit. And I've noticed when I just don't care, or that I'm not studying for tests that have come up or are coming up, that's what I notice that…depression is getting worse… [laughs]*

One individual explained that they commonly experience insomnia.

> *"If my symptoms came back, the first thing would be no sleep."*

In contrast, another individual would notice themselves to socially withdraw.

> *"I think it would be shutting myself out again. Because I got…I got to a point where I was just shutting everyone out. And I wasn't…like I was just shoving everything down, and not letting people in. And I think that the biggest pivotal point was when I came here and I was able to…open up. Open up and talk about how I'm feeling."*

Making mental health decisions

Participants consistently expressed wanting to be more involved in health care decision-making and planning. They also wanted to learn more about their diagnosis, what it means for them, their future, and why they are experiencing this. One individual expressed that listening and getting input from patients is essential for developing empathy and making a connection with them.

> *"If you don't get input from them, then you don't know what they're going through, you don't know how it is, you can't empathize with them."*

General perceptions of the healthcare system

Participants commonly expressed frustration with the way they feel viewed by the health care system and society. Emerging adults feel others (e.g., society, the health system) may not value their mental health needs as much as their physical needs. One individual felt frustrated that simply because she needed psychiatric medication, she felt others viewed her as less incapable.

> *"We need medicine, like we need help producing chemicals in our brain, because our brain doesn't make them the same way that regular people…make them, and but I mean that doesn't make us less of a person or less capable."*

3.5 DISCUSSION

To our knowledge, this is the first study to explore the life stories of emerging adults with symptoms of anxiety and/or depression. Interestingly, we found that the stories of these individuals varied considerably when considered as a whole, but potentially important/useful patterns emerged across the data. For instance, a majority of the participants described experiencing various stressful experiences during childhood and/or adolescence -- ranging from academic stress, social acceptance/anxiety, inter-familial conflict, verbal abuse, neglect and other traumas (e.g., experiencing homicide). The participants described coping with these challenges in various ways such as socially withdrawing and attempting to relieve acute distress by self-medicating with substances such as alcohol and/or cannabis; however, internalizing these distresses, rather than expressing these concerns to people close to them, was common.

A key finding included the identification of potential facilitators for obtaining mental healthcare. For example, several participants described memories of experiencing positive encouragement or outreach from an individual personally close to them (e.g., a parent, partner, or high school counselor). Moreover, very few of the participants described seeking treatment without some type of social support. The ones that did seek care on their own described "hitting rock bottom" before they finally sought care, which commonly left them at high-risk self-harm (e.g., substance misuse or suicidal ideation). Additionally, the participants provided unique accounts of what "recovery" and "relapse" meant to them, including rich discussion around concerns not being work or perform academically. These fears about their illness appeared from the interviewer's perspective to potentially negatively impact their attitude and self-worth. Generally, the participants conveyed a strong desire to be independent, self-sufficient, and able to contribute to society. This finding is congruent with previous literature suggesting that emerging adults with mental health symptoms may focus on hope and coping.[35]

Barriers to obtaining care include several experiences of stigma, shame, preference for self-reliance, and potentially low health literacy. Almost all participants expressed a desire to be involved in healthcare decisions and planning, including a desire to learn more about their health conditions and/or symptoms. One individual expressed difficulty remembering clinical conversations, and a visual diagram or reminder may be helpful. Another key finding of this study was learning of participant's desire to become more involved in their mental health decision-making. This is supported by recent evidence suggesting that patient engagement may improve when the individual's values, needs, and concerns are considered/valued by friends, family members and clinical staff.[26, 36] Our findings concerning perceptions of barriers to care in emerging adults with anxiety or depression build upon previous literature.[17, 18, 35-39] Our results provide a rich understanding of the life experience of emerging adults with anxiety and/or depression, including an illustration of the treatment seeking/utilization process, and provision of discussion for improving access to care and clinical decision-making.[40-42] Moreover, this study provides a rich description regarding how emerging adults may cope with symptoms of anxiety, which appears to be largely absent from the literature.

In comparison with the literature involving other age groups[43, 44], our findings may show that the coping patterns of emerging adults with symptoms of anxiety and depression may be more similar

to adolescents than older adults. For example, both adolescents and emerging adults are more likely to prefer self-reliance and tend to be more reluctant to seek mental healthcare than older age groups, and may value for autonomy in decision-making.[43, 44] These distinct behavioural observations have been further supported by recent advances in neuroscience, which have revealed striking distinctions in the neurobiology of emerging adults in comparison to older adults. For instance, neuromaturation (i.e., cortical grey matter pruning and increased white matter connectivity) does not finalize until approximately 25 years of age[45, 46], with heterogeneity in this process related to biological sex.[47] This knowledge, may partially explain why emerging adults (particularly males) may commonly engage in higher risk-taking behaviours (e.g., substance use), and may be hesitant to seek treatment.[4, 48]

3.5.1 Limitations

We note several limitations of this study. First, only individuals who voluntarily sought mental health care were included in this study, limiting any generalizability only to emerging adults who may be motivated to seek professional mental healthcare in Alberta. We planned to address this issue by recruiting emerging adults who may not use/access conventional mental health care by recruiting from two harm reduction centres, but this attempt was unsuccessful largely due to individuals not meeting our *a priori* eligibility criteria.

It is common in narrative inquiry to conduct a series of interviews and co-construct the results with the participants.[49, 50] However, in-person follow-up interviews with participants were not possible due to COVID-19-related restrictions. Phone or online interviews were considered in lieu; however, the quality of the data participants share may vary depending on the mode used to collect it.[51, 52] The research team subsequently decided that additional in-person interviews would not be feasible/necessary and phone/online interviews would most likely negatively impact the data quality. Future research may address this issue by conducting focus groups involving this population exploring these findings and obtaining feedback.

Additionally, the interviewer noted that in moments when the conservation started to stall, that probing questions were used around the topic of shared decision-making, relapse and recovery. Moreover, the data around these questions likely did not emerge naturally from the participant as these probes were planned *a priori* by the interviewer. Although, the interviewer was careful to not provide his own views on these topics, it is difficult to confirm that no interviewer or participant

biases occurred in these discussions which may skew the results. Additional research is suggested to enhance verification of these findings.

3.5.2 Implications

Despite these limitations, our main findings suggest that emerging adults in treatment for mental health conditions may desire to have more of an active role in mental health-related decision-making and planning. These findings may be used as a preliminary framework for informing of the design of mental health services tailored to the needs/values of emerging adults. Research that highlights the lived experience and individual stories of emerging adults may help guide future research for developing targeted campaigns for reducing implicit biases observed from healthcare providers and the general population.[23, 24, 26, 36, 39] Additionally, increased awareness of this and related research may help emerging adults feel that their individual experiences are valued, which may in turn promote outcomes such as increased self-esteem, therapeutic alliance, treatment retention, and may reduce internalized stigma.[26, 36, 53] Additional research involving emerging adults with and without symptoms of anxiety and/or depression, and those who have not sought mental healthcare, is recommended to inform person-centred healthcare efforts.

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3.7 ADDITIONAL INFORMATION

3.7.1 Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

3.7.2 Contributors

The first author and the senior author developed the research questions and methods. The co-authors provided substantial input into the development of the research questions and methods. The first author collected and analyzed the data and drafted the manuscript. Each author provided feedback drafts of the manuscript. All authors approved the final version of this manuscript.

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3.8 TABLES

3.8.1 TABLE 1. Participant demographic data

Variable	Inpatients	Outpatients	Total
Demographic characteristics			
N participants	5 (41.7)	7 (58.3)	12
Age, years (mean ± SD)	21.8 (2.17)	21.7 (2.14)	21.8 (2.05)
Gender, n (%) male	3 (60.0)	2 (28.6)	5 (41.7)
Ethnicity n (%)			
Caucasian	3 (60.0)	3 (42.9)	6 (50.0)
Aboriginal	2 (40.0)	1 (14.3)	3 (25.0)
Chinese	0	1 (14.3)	1 (8.33)
Filipino	0	1 (14.3)	1
Unspecified	0	1 (14.3)	1
Marital status n (%)			
Legally married or common law	0	0	0
Total family income n (%)			
Less than $20,000	2 (40.0)	4 (57.1)	6 (50.0)
$20,000 to $34,999	1 (20.0)	0	1 (8.33)
$35,000 to $49,999	0	0	0
$50,000 to $74,999	0	0	0
$75,000 to $99,999	1 (20.0)	2 (28.6)	3
$100,000 to $149,999	0	1 (14.3)	1 (8.33)

$150,000 or more	0	0	0
Missing	1 (20.0)	0	1 (8.33)
Education n (%)			
Less than high school degree	0	1 (14.3)	1 (8.33)
High school degree or equivalent	3 (60.0)	2 (28.6)	5 (41.7)
Some post-secondary education but no degree	2 (40.0)	4 (57.1)	6 (50.0)
Registered apprenticeship or other trades certificates or diploma	0	0	0
Associate degree	0	0	0
Bachelor degree	0	0	0
Graduate degree	0	0	0
Clinical outcomes n (%)			
Diagnosed mental health condition	5 (100)	6 (85.7)	11 (91.7)
Prescribed psychiatric medication	5 (100)	5 (71.4)	10 (83.3)
Reporting use of psychoactive substances	3 (60.0)	3 (42.9)	6 (50.0)
Report using psychoactive substances or alcohol to self-medicate distress or symptoms	4 (80.0)	3 (42.9)	7 (58.3)
HADS ≥8 anxiety	3 (60.0)	6 (85.7)	9 (75.0)
Missing	1 (20.0)	1 (14.3)	2 (16.7)
HADS ≥8 depression	3 (60.0)	4 (57.1)	7 (58.3)
Missing	1 (20.0)	1 (14.3)	2 (16.7)

HADS ≥8 anxiety and depression	3 (60.0)	4 (57.1)	7 (58.3)
Missing	1 (20.0)	1 (14.3)	2 (16.7)

CHAPTER 4: The relationship between shared decision-making, patient health engagement and health-related quality of life among emerging adults in community mental health and primary care settings: A cross-sectional study

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This manuscript has been submitted to a peer-reviewed journal

4.1 ABSTRACT

It is hypothesized that shared decision-making (SDM) may be associated with outcomes such as patient health engagement (PHE), health-related quality of life (HRQL) and/or anxiety/depression in emerging adults (18-29 years). A cross-sectional study was conducted in 14 outpatient healthcare settings in Alberta exploring these potential relationships. Thirty-one healthcare providers and 42 emerging adult patients were analyzed. SDM was not associated with PHE, anxiety/depression or HRQL; however, limited variability within the SDM scores hampered the analysis. The presence of anxiety/depressive symptoms and low HRQL was associated with lower PHE among patients during a clinic visit. Implications for future research are discussed.

Keywords: patient-centered care, primary health care, mental health, anxiety, depression, depressive disorder, depression, patient participation, young adult

4.2 INTRODUCTION

Increasing patients' health knowledge, capacity, and activation is associated with improved health outcomes and reduced health system costs.[1, 2] Evidence suggests that adults with higher patient health engagement (PHE)[2] may be more likely to become activated, adhere to prescribed medications[2], and may be more likely to successfully navigate intricate health services.[3] Graffigna and colleagues [3] characterized PHE as "patients' motivation and self-determination to become an active player in the healthcare journey."[2-5] Some health scholars suggest that patients who are active in their health goal setting, engaged in health decision-making, and have competent knowledge about their illness, may be likely to experience improvements in patient-reported outcomes such as health-related quality of life (HRQL).[1, 2, 6] Systematic reviews suggest that poor engagement in healthcare is associated with deleterious outcomes among young individuals with mental illnesses.[7, 8] For instance, unsatisfactory patient health engagement may be linked to the disproportionately high rates of anxiety, depressive, and substance use disorders reported among young adult populations.[9, 10] Epidemiological data suggest that emerging adults (i.e., individuals approximately 18-29 years) experience among the highest rates of anxiety and/or depression of any adult age group[11, 12], and may be the least likely to seek mental health care or remain engaged in treatment.[13]

In recent years, shared decision-making (SDM) has been considered as a promising strategy for enhancing patient participation in health decision-making in both primary care and mental health services, and may be associated with PHE.[14-17] SDM is characterized by Elwyn and colleagues as "an approach where clinicians and patients share the best available evidence when faced with the task of making decisions, and where patients are supported to consider options to achieve informed preferences.[18] SDM, as a construct, aligns within the theoretical frameworks of patient or person-centred care [19] and personalized medicine[14] and has been touted by some scholars are the "pinnacle of patient-centred care."[19] Recent randomized controlled trials suggest that SDM may improve patient-reported outcomes such as satisfaction with care and treatment adherence in adults with chronic physical illnesses such as hypertension, cardiovascular disease, and diabetes[20, 21], and common mental illnesses such as depressive disorders.[22-24]

Previous research suggests that emerging adults may prefer more autonomy in their health decisions, self-management of mental health symptoms, and may reject paternalistic approaches to their health compared to other age groups.[25, 26, 27, 28] Several authors have suggested that it may be worthwhile to investigate novel ways to enhance patient involvement, activation, and PHE as this may help encourage early health service utilization, diagnosis, and adequate treatment of mental health concerns in young people.[8, 29, 30] To our knowledge, no research studies have yet explored possible links between SDM and PHE in emerging adults with anxiety and/or depression.[2] However, there is some evidence to suggest that adults with mental illnesses such as anxiety disorders may require a higher level of psychosocial support to facilitate their decision-making needs.[31] For instance, in a recent online survey, the authors found that 55% of adults 18 to 77 years with anxiety disorders preferred using SDM during clinical encounters, while the remainder preferred a more passive role.[31] It is unclear whether these results are generalizable to emerging adults 18-29 years. Better understanding of the barriers and facilitators for enhancing PHE may help guide service development and inform clinical practice.[1, 13]

4.2.1 Objective

The objective of our study was to explore whether SDM during a single clinic visit was associated with PHE and/or HRQL in emerging adults who sought care in primary care or outpatient mental health settings. Based upon previous literature, we hypothesized that both PHE and HRQL would be positively correlated with SDM.

4.3 METHODS

4.3.1 Study design

A multicentre cross-sectional study was conducted. A subset of data focused on the age range of interest was obtained from a larger pan-provincial study on SDM in adults seen in primary care or mental health settings in Alberta, Canada. Ethics approval was granted by the Health Research Ethics Board at the University of Alberta (application number: Pro00066937). The Strengthening of the Reporting of Observational Studies (STROBE)-Statement was used to guide reporting of the results.[32]

4.3.2 Setting

Participants (healthcare providers and patients) were recruited from six community-based primary care clinics and eight addiction and mental health clinics across all five health service zones of the province of Alberta, Canada. The data were collected from January to December 2019.

4.3.3 Participants

After ethics approval and consent from clinic managers, licensed healthcare providers were recruited on a voluntary basis via email. After informed consent, healthcare providers were asked to identify any/all patient participants who met the eligibility criteria. All patients had provincial health insurance, which fully covered the costs of the clinic visits. All participants were recruited on a voluntary basis and were free to discontinue participation at any time. The participants did not receive reimbursement or compensation for their participation.

4.3.3.1 Eligibility criteria

Any healthcare provider who was licensed in Alberta was eligible for this study. Emerging adult patients (18-29 years of age) who voluntarily sought and obtained health services at a participating primary care or outpatient mental health setting in Alberta were also eligible. All participants were required to provide informed written consent, be able to participate without a proxy, and understand, write, and speak English language. We included patients at any point in their treatment trajectory. Patients were excluded who, in the opinion of their health care provider, were currently experiencing a mental health crisis (i.e., a potential danger to self or others within the last 7 days prior to the clinic visit), or whose clinic visit was mandated for any reason (e.g., drug-related pre-trial diversion program).

4.3.4 Data collection

Following ethics approval from the Health Research Ethics Committee at the University of Alberta and operational approval from Alberta Health Services, the research assistant met with the health care providers at each clinic, answered any questions, and obtained written from those willing to participate. Participating health care providers told eligible patients about the study and referred

those who were interested in learning more about the study to the research assistant. The research assistant answered any questions and obtained written consent from patients willing to participate.

After informed consent, the participating healthcare providers completed a sociodemographic form including age, ethnicity, professional designations, and when professional training was completed. After each clinic visit with each participating patient, the healthcare provider completed the healthcare provider version of the Alberta Shared decision maKing Measurement Instrument (ASK-MI) on paper.

After the clinic visit with the participating healthcare provider, each participating patient was invited to complete a series of questionnaires on an encrypted electronic tablet. A sociodemographic form queried participants' age, gender, marital status, ethnicity, level of education, total household income, and the presence of any diagnosed chronic health conditions. Then, the patients completed a series of questionnaires measuring SDM, PHE, HRQL, and symptoms of anxiety and depression. The research assistant aided participants in use of the tablet when requested. All collected data were stored in the Health Research Data Repository at the Faculty of Nursing, University of Alberta. The data were anonymized and only available to the research team. The questionnaires are described in more detail below.

4.3.5 Variables

4.3.5.1 Shared decision-making

The ASK-MI was used to measure healthcare providers and patients' perception of SDM.[33] The ASK-MI is a 6-item dyadic questionnaire that uses a Likert scale (strongly agree to strongly disagree), with scores ranging from 6-36. The internal consistency (Cronbach's alpha) for ASK-MI-patient version is 0.996 and ASK-MI-healthcare provider version is 0.950.[34] Both versions are completed independently by both the patient and their healthcare provider following the consultation. The ASK-MI scores of dyads are calculated as follows: If *both* the health care provider and the patient assigned a score between 6 and 12, the SDM was considered "excellent", if both the health care provider and the patient assigned scores between 13 and 24 the SDM was considered "acceptable." If both the health care provider and the patient assigned a score between 25 and 36, the SDM was considered "unacceptable." If scores of the health care provider and

patient differ, the visit is assigned the lower SDM score. The ASK-MI PATIENT version is attached in **SUPPLEMENTARY FIGURE 1**.

4.3.5.2 Patient health engagement

Patient health engagement (PHE) was measured using the Patient Health Engagement scale (PHE-S), which is a validated questionnaire used to assess the "level of a patient's knowledge and competence to deal with their own health condition" and the "degree of emotional elaboration and adjustment reached by the patient concerning his/her own health condition when engaging in health management."[2, 4] The PHE-S is comprised of five questions with response options converting to an ordinal scale of 1-4, with 1 indicating poor engagement (i.e., "blackout") and 4 indicating optimal engagement (i.e., "eudiamonic project").[2]

4.3.5.3 Symptoms of anxiety and/or depression

Symptoms of anxiety and/or depression were assessed using the valid and reliable Hospital Anxiety and Depression Scale (HADS).[35, 36] The HADS is split into two sections (HADS-A and HADS-D). Clinically significant symptoms of anxiety were defined as scores of ≥8 on HADS-A and clinically significant symptoms of depression were defined as scores of ≥8 on HADS-D. A systematic review confirmed that these cut points have a high positive predictive value for identifying individuals with anxiety and/or depressive disorders.[37]

4.3.5.4 Health-related quality of life

Health-related quality of life (HRQL) was measured using the EuroQol-5D-5L (EQ-5D-5L)[38], which measures HRQL on five domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, each with five levels, producing a possible 3,125 health state combinations ranging from 11111 (full health) to 55555 (worse than death). A level 1 response represents "no problem," level 2 "slight problems," level 3 "moderate problems," level 4 "severe problems," and level 5 "extreme problems" or "unable to perform".[39, 40] These values were converted into a dimension index based on Canadian population. The values are converted to a continuous scale ranging from 55555 = -0.15 (worse than death) to 11111 = 0.95 (full health)".[39-41] We then dichotomized the HRQL dimension index scores based on the Alberta average for the EQ-5D-5L

which is 0.84.[38, 42] Using the Canadian minimally important difference value of 0.05[41],we then reduced the cut point to ≥0.79 to differentiate between normal and abnormal. Specifically, EQ-5D-5L values above 0.79 were considered normal or above normal, and values below 0.79 were considered below normal. Additionally, the EQ-5D-5L records an individual's perception of overall health using a single visual analogue sliding scale (VAS). The VAS is recorded on a continuous scale of 0-100, with zero equal to worst health and 100 equals full health. Only the dimension index scores were used for our primary analyses, and the visual analogue scale was reported descriptively.

4.3.6 Data analysis

Data were cleaned and then analyzed using SPSS version 23 (IBM Statistics). Pearson chi-square, and Spearman's *Rho* tests were used to analyze the data, with the significance level (alpha) set to P=0.05. Due to the small sample size obtained, any missing data were excluded from the analysis.

4.4 RESULTS

4.4.1 Study characteristics

FIGURE 1 displays the study flow chart. Data were successfully obtained from urban, rural and remote regions of a geographically large province in western Canada, including six primary care settings and eight mental health settings. Thirty-one healthcare providers were recruited in total, with 20 from mental health clinics and 11 from primary care settings. Forty-two patients were recruited, with 10 patients from primary care settings and 32 from mental health settings.

4.4.2 Participant characteristics

4.4.2.1 Healthcare providers

Thirty-one healthcare providers were recruited in total, with 20 from mental health clinics and 11 from primary care settings. **TABLE 1** displays the complete baseline sociodemographic data obtained from the participating healthcare providers.

4.4.2.2 Patients

Forty-two patients were recruited, with 10 patients from primary care settings and 32 from mental health settings. The mean age of the patients was 24.1 years (SD = 3.0 years). HADs criteria for anxiety was met for 73.8% (n=31) of the patients, followed by 40.5% (n=17) with depression and 38.1% (n=16) meeting the criteria for both anxiety and depression, 26.2% (n=11) did not meet the criteria for either condition. **TABLE 2** displays the complete baseline sociodemographic data obtained from the participating patients.

4.4.3 Main findings

4.4.3.1 Shared decision-making

TABLE 3 displays descriptive comparisons between healthcare providers and patients on rating the quality of SDM during a clinic visit. In 69% (n=29) of the sessions, both the health care provider and the patient rated SDM as excellent. In 31% (n=13) of the sessions, either the healthcare provider or the patient rated the SDM as acceptable. Neither a patient nor a healthcare provider rated SDM as unacceptable in any session. We found that healthcare providers and patients agreed on the quality of SDM as either excellent or acceptable on 69% (n=29) of the total visits (n=42).

TABLE 4 shows the main findings according to SDM. No significant relationship was observed between SDM and PHE, r=0.03, P=0.83. Clinically significant symptoms of anxiety and/or depression were not statistically significantly associated with SDM (X^2=0.09, P=0.76; X^2=0.74, P=0.39; X^2=0.43, P=0.51). HRQL was not associated with SDM (X^2=0.15, P=0.70). SDM ratings did not differ by setting (mental health vs. primary care) (X^2=0.006, P=0.94).

4.4.3.2 Patient health engagement

TABLE 5 shows the main findings according to PHE. We found that clinically significant symptoms of anxiety and/or depression were negatively associated with PHE (r=-0.59, P<0.001; r=-0.46, P=0.002; r=-0.50, P=0.001). HRQL was positively associated with PHE (r=0.62, P<0.001).

4.5 DISCUSSION

Most studies of SDM to date have focused on its use during the selection of treatment options. To our knowledge, this is the first study to investigate how SDM relates to outcomes such as PHE, HRQL, and anxiety and depression during a routine clinic visit in emerging adults. We found that clinically significant symptoms of anxiety and/or depression were negatively associated with PHE, implying the presence of mental health symptoms may play a role in whether a patient will become engaged with the management of their mental health care planning or treatment. These findings are consistent with other studies suggesting that symptoms related to anxiety and/or depression may pose a barrier to PHE.[7, 10, 43, 44] For example, authors of a systematic review in 2008 found that cognitive impairment is common among young adults with anxiety and depressive disorders.[43] The authors; however, noted that the level of impairment may vary considerably among individuals.[43]

In our study, the difference between excellent and acceptable SDM was not associated with the level of PHE or HRQL. This may have occurred for a few reasons: i) the small sample size may have limited power to detect a difference; ii) the limited variability in SDM ratings, including no "unacceptable" scores, may have been insufficient to detect a difference; iii) healthcare provider behavior may be more related to the quality of SDM than patient characteristics; iv) the quality of SDM may not have an immediate impact on outcomes, and may take time to see any results associated with the health decisions facilitated by SDM.

Other authors have reported associations between SDM and various patient-reported health outcomes. For example, the authors of randomized controlled trials of adults 18-64 years, reported that SDM (or collaborative care with SDM) was positively associated with patient- satisfaction with care.[22-24, 45-47] Each of these studies, however, measured health outcomes longitudinally. Other authors have suggested that because SDM is heavily influenced by the relationship between a given patient and their health care provider, one may not get an accurate measure of SDM or its impact on health outcomes until after several visits. Longitudinal studies of SDM could be used to track the development of SDM between a patient and his or her health care provider over time and assess the potential impact on PHE and HRQL.

It is important to learn more about the links between PHE and SDM among emerging adults with symptoms of anxiety and/or depression because of their potential impact on health outcomes such

as treatment adherence and quality of life. There is some evidence that when patients' unique goals are addressed, treatment engagement improves in young adults with mental health conditions.[7] In a systematic review of 23 studies[44], the authors found that an improved client and clinician alliance was associated with improved treatment adherence in mental health care. Treatment adherence was not measured in our study, but we plan to include it in future longitudinal research.

A better understanding of the barriers and facilitators to PHE has been identified as a priority for improving treatment adherence, patient satisfaction, and promotion of person-centred care.[48-50] This study adds to the literature by demonstrating that clinically significant symptoms of anxiety and/or depression and low HRQL may pose barriers for being emotionally ready to engage in therapy and manage these conditions.

There are several strengths of this study. First, we successfully obtained data from urban, rural, and remote regions of a geographically large province in Canada. Second, the instruments used were valid and reliable, and the data collection methods were efficient and highly secure. Third, this study provides novel evidence about an understudied population.

4.5.1 Limitations

Several limitations in this study warrant a cautious interpretation of the results. First, a temporal relationship cannot be ascertained between the study variables using a cross sectional design.[51] Secondly, a small sample size was obtained as relatively few individuals aged 18-29 participated in the larger study, in keeping with the generally low rates of health care utilization among emerging adults.[13] The small sample size precluded additional statistical analyses that may have identified an independent associations among variables while controlling for potentially confounding variables, such as gender, socioeconomic status, family income, or educational attainment. We hypothesize that these variables may also be related to PHE, anxiety and/or depression, and HRQL. Furthermore, a small sample size prevented us from comparing outcomes between primary care and mental health settings.

The lack of longitudinal data precluded any ability to see the possible impact of SDM over time. Larger longitudinal studies controlling for potentially confounding variables are required to assess a possible effect associated with SDM on health outcomes. The variability of the obtained SDM

scores were limited, which made it difficult to ascertain a possible relationship between PHE, HRQL, and SDM. This may be partially explained by a volunteer bias such that individuals who were more interested in SDM may have chosen to participate in the study, leading to a ceiling effect of high SDM scores. The findings of this study should be viewed as preliminary and used to help guide future research in this field.

4.5.3 Conclusions

This study adds to the literature related to person-centred care and SDM in the context of mental health in emerging adults. We recommend larger-scale prospective studies to further investigate the relationship between SDM, PHE, and HRQL, accounting for the potential impact of the use of SDM, through a series of meetings over time. Qualitative studies may be useful for exploring the perceptions of emerging adults regarding their willingness to seek and/or stay engaged with health care.[52]

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4.7 ADDITIONAL INFORMATION

4.7.1 Contributions

All authors have made significant intellectual contributions to the development of this manuscript. TM, KO, and SV developed the initial research questions and methods. KO, AA, RL, XL assisted in refinement of the research questions, development of the methods, and revisions of the manuscript. TM analyzed the data. All authors have provided substantial intellectual input and have approved the final version of this manuscript.

4.7.2 Data access

Data may be available upon request.

4.7.3 Acknowledgements

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4.7.4 Conflict of interest disclosure

The authors declare that there is no conflict of interest.

4.7.5 Funding

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4.8 TABLES

4.8.1 TABLE 1. Healthcare provider sociodemographic characteristics

Variable	Value
Demographic characteristics	
N participants	31
Age, years (mean ± SD)	40.9 (8.58)
Age, range (years)	27-58
Gender, n (%) male	7 (22.6)
Clinical setting n (%)	
Primary care	11
Addiction and mental health	20
Setting location by Alberta Health Zone n (%)	
North	5 (16.1)
Edmonton	14 (45.2)
Central	3 (9.7)
Calgary	7 (22.6)
South	2 (6.5)
Profession n (%)	
Physicians	7 (22.6)
Registered nurses (including psychiatric nurse)	4 (12.9)
Mental health therapists (e.g., counselor or psychologist)	8 (25.8)

Social workers	5 (16.1)
Dieticians	3 (9.68)
Physical or occupational therapists	4 (12.9)

4.8.2 TABLE 2. Patient sociodemographic characteristics

Variable	
Demographic characteristics	
N participants	42
Age, years (mean ± SD)	24.1 (3.0)
Gender, n (%) male	9 (22.0)
Gender, n (%) other	1 (2.43)
Missing, n (%)	2 (4.89)
Ethnicity, Caucasian n (%)	23 (54.8)
1 ≥ reported chronic conditions n (%)	32 (76.2)
Missing, n (%)	1 (2.4)
Marital status n (%)	
Legally married or common law	7 (16.7)
Missing, n (%)	2 (4.8)
Total family income quintile n (%)	
Less than $20,000	11 (26.2)
$20,000 to $34,999	4 (9.5)
$35,000 to $49,999	4 (9.5)
$50,000 to $74,999	6 (14.3)
$75,000 to $99,999	6 (14.3)
$100,000 to $149,999	3 (7.1)
$150,000 or more	1 (2.4)

Missing	7 (16.7)
Employment	
Employed, working 40 or more hours per week	9 (21.4)
Employed, working 1-39 hours per week	14 (33.3)
Not employed, looking for work	8 (19.0)
Not employed, not looking for work	2 (4.8)
Retired	0
Unable to work	9 (21.4)
Education	
Less than high school degree	5 (11.9)
High school degree or equivalent	13 (31.0)
Some post-secondary education but no degree	13 (31.0)
Registered apprenticeship or other trades certificates or diploma	3 (7.1)
Associate degree	1 (2.4)
Bachelor degree	6 (14.3)
Graduate degree	1 (2.4)
Clinical setting	
Primary care	10 (23.8)
Addiction and mental health	32 (76.2)
Setting location by Alberta Health Zone	

North	7 (16.7)
Edmonton	21 (50.0)
Central	3 (7.1)
Calgary	9 (21.4)
South	2 (4.8)
Clinical outcomes	
HADS ≥8 anxiety n (%)	31 (73.8)
HADS ≥8 depression n (%)	17 (40.5)
HADS ≥8 anxiety and depression n (%)	16 (38.1)
EQ-5D dimension index (mean ± SD)	0.72 (0.21)
EQ-5D VAS (mean ± SD)	68.3 (18.1)
PHE median score ≥ 3 n (%)	25 (59.5)

4.8.3 TABLE 3. Quality of shared decision-making during the clinic visit as rated by healthcare providers, patients and dyad

Status	**N**	**Rating**	**N (%)**
Healthcare providers	31	Excellent	32 (76.2)
		Acceptable	10 (23.8)
		Unacceptable	0
Patients	42	Excellent	39 (92.9)
		Acceptable	3 (7.1)
		Unacceptable	0
Dyad	42	Excellent	29 (69.0)
		Acceptable	13 (31.0)
		Unacceptable	0

4.8.4 TABLE 4. Shared decision-making ratings by anxiety and/or depression, health-related quality of life and setting

Construct	**Measurement**	**Rating**	**Shared decision-making (binary)**		**Total**	**Test statistic**	**P value**
			Acceptable	Excellent			
Anxiety	HADs-A	Normal	3	8	11	X^2=0.09	0.76
		Abnormal	10	21	31		
Depression	HADs-D	Normal	9	16	25	X^2=0.74	0.39
		Abnormal	4	13	17		
Comorbid anxiety and depression	HADs-AD	Normal	9	17	26	X^2=0.43	0.51
		Abnormal	4	12	16		
Health-related quality of life	EQ-5D-5L	Normal	5	13	18	X^2=0.15	0.70
		Abnormal	8	16	24		
Setting	Location of data collection	Mental health	10	22	32	X^2=0.01	0.94
		Primary care	3	7	10		

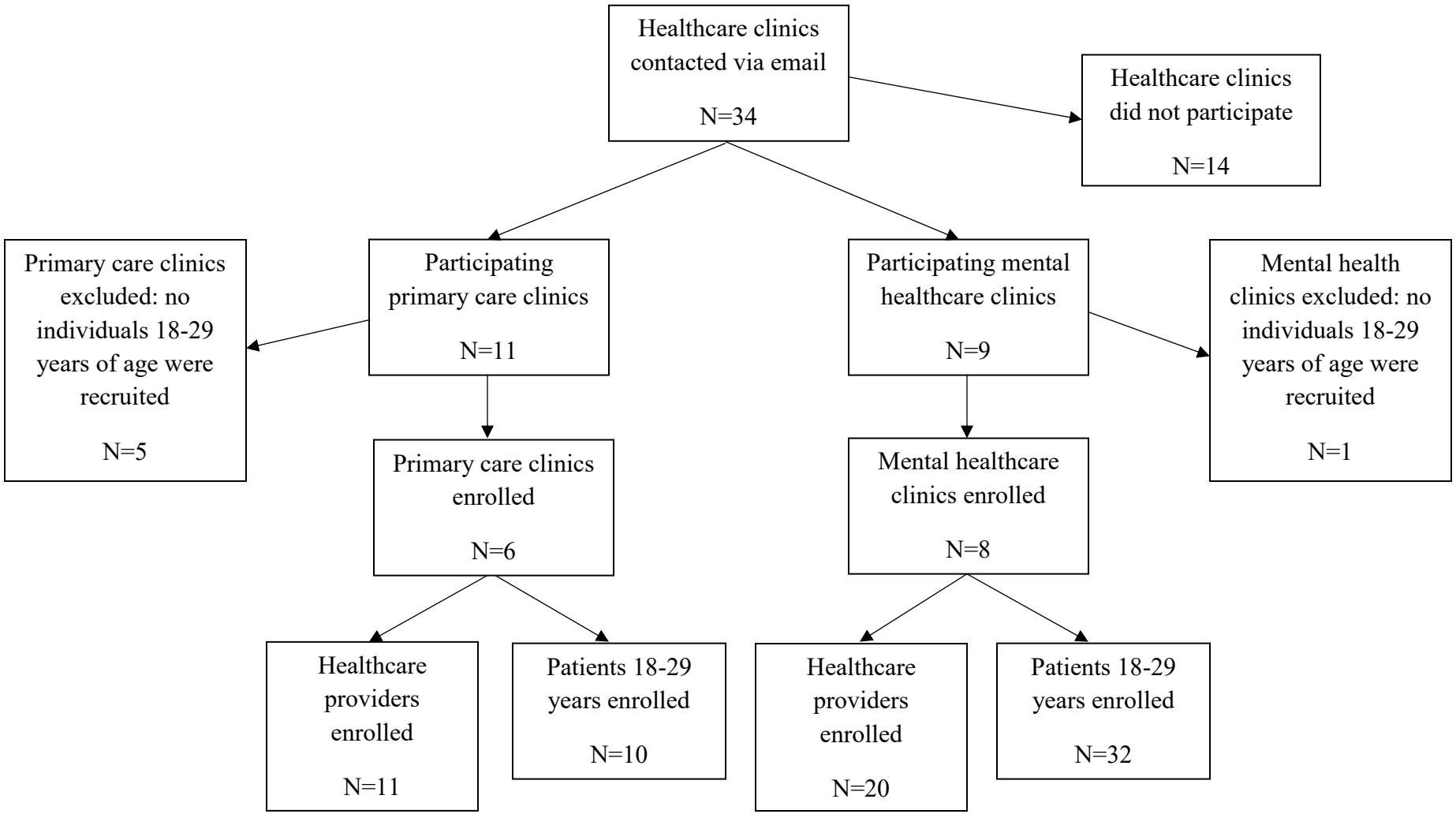
4.8.5 TABLE 5. Patient health engagement ratings by shared decision-making, anxiety and/or depression and health-related quality of life

Construct	**Measurement**	**Rating**	**Patient health engagement (quartile)±**				**Totals**	**Test statistic**	**P value**
			Blackout	Arousal	Adhesion	Eudaimonic project			
SDM	ASK-MI Dyad	Acceptable	1	5	7	0	13	r=0.03	0.83
		Excellent	4	9	13	3	29		
Anxiety	HADS-A	Normal	0	0	8	3	11	r=-0.59	<0.001**
		Abnormal	5	14	12	0	31		
Depression	HADS-D	Normal	1	6	15	3	25	r=-0.46	0.002**
		Abnormal	4	8	5	0	17		
Comorbid anxiety and depression	HADS-AD	Normal	1	6	16	3	26	r=-0.50	0.001**
		Abnormal	4	8	4	0	16		
Health-related quality of life	EQ-5D-5L	Normal	0	2	13	3	4	r=0.62	<0.001**
		Abnormal	5	12	7	0	4		

Footnotes: ± Patient health engagement is measured on an interval scale using quartiles, ranging from lowest to highest (blackout being lowest and eudaimonic project being the highest)

*denotes statistical significance at the 0.05 level. **denotes statistical significance at the 0.01 level**4.9.1 FIGURES**

4.9.1.1 FIGURE 1. Study flow chart



4.10 SUPPLEMENTARY FILES

4.10.1 SUPPLEMENTARY FIGURE 1. Alberta Shared Decision Making Measurement Instrument (ASK-MI) - Patient/client Version

Alberta Shared Decision Making Measurement Instrument (Patient/Client)

This purpose of this tool is to gather information about shared decision making between you and your health care provider. A shared decision is one that you and your health care provider make together, after considering options based on the best available evidence and your preferences. For the purposes of this tool, a health care provider is anyone with whom you have a clinical appointment regarding your health, such as a physician, a nurse, a nurse practitioner, a dietician, a social worker, a mental health therapist, or an exercise specialist.

Instructions: Put an x in each row to indicate how strongly you agree or disagree.

	Strongly Agree	Mostly Agree	Moderately Agree	Slightly Agree	Mostly Disagree	Strongly Disagree	Not Applicable
Q1. My health care provider and I agreed on the main concern(s) and focus of the visit.							
Q2. My health care provider and I worked together to make a plan that addressed my preferences.							
Q3. The plan that my health care provider and I made considered my wishes and abilities.							
Q4. My health care provider checked that I understood the plan.							
Q5. My health care provider checked if I could follow the plan between now and my next appointment.							
Q6. I agreed with the plan my health care provider and I made.							

Please rate the shared decision making for this visit by placing an X next to the word that best describes your rating.

____ Excellent
____ Acceptable
____ Unacceptable

Please indicate whether you involved family or friends in a discussion of your treatment options.

____ No
____ Yes

4.10.2 SUPPLEMENTARY TABLE 1. Relationship between health-related quality of life and symptoms of anxiety and depression.

Construct	**Measurement**	**Rating**	**Health-related quality of life**		**Total**	**Test statistic**	**P value**
			Abnormal	Normal			
Anxiety	HADs-A	Normal	1	10	11	X^2=14.1	P<0.001**
		Abnormal	23	8	31		
Depression	HADs-D	Normal	11	14	25	X^2=4.36	P=0.037*
		Abnormal	13	4	17		
Comorbid anxiety and depression	HADs-A and D	Normal	11	15	26	X^2=6.13	P=0.013**
		Abnormal	13	13	16		

Footnotes: *denotes statistical significance at the 0.05 level. **denotes statistical significance at the 0.01 level.

CHAPTER 5: Preexisting anxiety and/or depressive disorders and risk of opioid use disorder in emerging adults: a case-control study

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5.1 ABSTRACT

Background: Anxiety, depressive, and opioid use disorders (OUD) are common in emerging adults and are associated with high rates of morbidity and mortality. A temporal relationship has not been formally established between these disorders.

Objective: To investigate whether previously diagnosed anxiety and/or depressive disorders are associated with subsequent OUD diagnoses in emerging adults (18-25 years).

Methods: An age/sex-matched case-control study was conducted using administrative health data from Alberta, Canada. Cases were required to have an administrative record of OUD, and be 18-25 years on April 1, 2018 for eligibility. Conditional logistic regression was used to calculate adjusted odds ratios (aOR). We controlled for alcohol-related disorders, several dispensed medications (e.g., opioid analgesics) and sociodemographic covariates in the analysis.

Results: We identified N=1,848 cases and N=7,392 controls. The following previously diagnosed mental health disorders were associated subsequent OUD after adjusting for additional covariates: Anxiety disorders, aOR=2.53 (95% CI=2.16 – 2.96); depressive disorders, aOR=2.20 (95% CI=1.80 – 2.70); concurrent anxiety and depressive disorders, aOR=1.94 (95% CI=1.56 – 2.40). Post-hoc analyses revealed the following concurrent disorders were associated with subsequent OUD: anxiety and alcohol-related disorders, aOR=5.22 (95% CI=4.03 – 6.77); depressive and alcohol-related disorders, aOR=6.47 (95% CI=4.73 – 8.84); anxiety, depressive and alcohol-related disorders, aOR=6.09 (95% CI=4.41 – 8.42).

Interpretation: Previously diagnosed anxiety and/or depressive disorders show a strong association with subsequent OUD in emerging adults. However, diagnosis of both conditions did not pose an additive risk of subsequent OUD diagnosis. Co-occurring alcohol-related disorders posed a substantive additive risk of subsequent OUD diagnosis Clinical and policy implications are discussed.

5.2 INTRODUCTION

Opioid use disorder (OUD) is defined by the Diagnostics and Statistics Manual 5th (DSM-5) Edition as the compulsive, non-medical use of opioids (e.g., heroin, fentanyl), persisting despite adverse consequences to one's daily life and/or functioning within a 12-month period.[1,2] OUD is associated with epidemic mortality rates worldwide due to unintentional opioid-related overdoses or poisonings[3,4], corresponding to a mortality rate of 48.6 per 1,000 person-years as identified in one longitudinal study.[5] Since 2015, the incidence rate of opioid-related deaths has become a leading cause of preventable death in North America, with incident rates over 10-20 per 100,000 person-years in many geographical areas[6], surpassing the incidence rate of motor vehicle fatalies.[7,8]

Emerging adulthood (i.e., individuals 18-25 years) are at substantial risk of OUD.[9,10] From 2002 until 2014, the prevalence of OUD increased from 12% to 15.1% among emerging adults who used opioids non-medically.[11] Notably, a majority of these individuals did not develop OUD[11], suggesting that other variables besides non-medical opioid use may be associated with the pathogenesis of OUD. Better understanding of the pathogenesis of OUD may help inform public health practices, policy and prevention efforts. However, the body of research around this topic is mixed. Early and prolonged exposure to prescribed opioid analgesics is commonly reported to increase the risk of OUD.[12] It is also widely known that chronic mental health conditions such as anxiety and/or depressive disorders are highly comorbid with OUD, but it is clear whether these conditions are associated with subsequent OUD diagnoses in emerging adults. For example, a large-scale survey in the United States reported that 19.97% of adult respondents diagnosed with a mood disorder met criteria for a substance use disorder within the last 12-months.[13]

There is emerging evidence suggesting that chronic preexisting mental health conditions may be associated with the onset of OUD in adults 18-65 years.[14-16] For example, an epidemiological study found that a history of trauma and/or mental health disorders were associated with increased odds of non-medical prescription opioid use in adults.[17] Moreover, a recent study linked anxiety sensitivity, defined as "misinterpreted cognitive, social, physical sensations/fears", with OUD severity.[18] Anxiety and/or depressive disorders are among the most prevalent mental health conditions in adolescents and emerging adults.[19-21] It is estimated that over 25% of individuals will experience a depressive episode during the emerging adulthood years.[22] As a result, we believe

that research exploring whether OUD is predicted by pre-existing anxiety and depressive disorder may help inform targeted public health interventions aiming which may reduce the incidence of OUD and opioid-related deaths.[23]

5.2.1 Objective

The objective of this study was to investigate whether previously diagnosed anxiety and/or depressive disorders were associated with subsequent diagnoses of OUD in emerging adults residing in Alberta, Canada on April 1, 2018.

5.3 METHODS

5.3.1 Study design

A population-based, age/sex-matched case-control study was conducted following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement guidelines.[24] This study was approved by the Health Research and Ethics Board at the University of Alberta (study number PRO00086565).

5.3.2 Setting

This study was conducted in Alberta, Canada (population 4.37 million). Alberta is a geographically large province in western Canada with a mix of urban, rural, and remote communities. There is one single-payer health care system that provides health coverage to nearly all residents of Alberta. The study period was from January 1, 2007, until March 31, 2018.

5.3.3 Source population

All Albertans between the ages of 18-25 years on April 1, 2018, with continuous provincial insurance coverage between April 1, 2002, and March 31, 2019, were eligible for inclusion.

5.3.4 Data sources

The following six administrative databases were searched for relevant health data: (i) ambulatory care (e.g., emergency data); (ii) physician billing (e.g., primary care); (iii) inpatient (e.g., hospital data); (iv) Pharmaceutical Information Network was searched for records of dispensed medications from database inception (April 1, 2008) until March 31, 2018; (v) Provincial Registry (e.g.,

demographic data and coverage with the Alberta Health Care Insurance Plan); and (vi) provincial Opioid Dependency Programs (ODP) (i.e., outpatient treatment programs for people with OUD). Only de-identified data were provided to the research team.

5.3.5 Outcomes

The presence or absence of an OUD diagnosis was captured as 'yes, no,' which was determined as the binary outcome variable of 'cases and controls.'

5.3.5.1 Cases

Eligible cases required i) an incident diagnosis of an opioid-related disorder as defined by International Classification of Disease (ICD) codes in relevant databases or (ii) an admission to an ODP at any time during the study period. Records for OUD were obtained from April 1, 2002, to ensure cases did not have records of OUD prior to the study period. Individuals with an OUD diagnosis prior to January 1, 2007, were excluded. All eligible cases were included, eliminating selection bias. More detailed information can be found in **S1**.

3.5.5.2 Controls

Controls were defined as individuals without an administrative health record of OUD or ODP enrollment at any time during the study period. To reduce selection bias, controls were randomly selected from the source population and matched on a 1:4 case-to-control ratio. Records for controls were obtained until April 1, 2002 to ensure OUD was not diagnosed prior to the study period.

5.3.6 Exposure variables

Following the literature review, three classes of clinically relevant covariates were selected *a priori.* More detailed information can be found in **S2**.

5.3.6.1 Exposure variables of focal interest

1) Preexisting mental health diagnoses (i.e., occurring prior to OUD or the index date in controls)
    a. Anxiety disorders;

b. Depressive disorders;
c. Alcohol-related disorders;
d. Substance-related disorders.
e. The date and age of the initial diagnosis (collected only for descriptive purposes).

5.3.6.2 Potential confounding variables

2) Sociodemographic characteristics
    a. Age (years) defined by the date of birth;
    b. Biological sex at birth (male/female);
    c. Location of residence (urban or rural residence) determined by postal code;
    d. Material deprivation (quintile);
    e. Social deprivation (quintile).

The social and material deprivation indices were derived via postal code and measured using the Pampalon Material and Social Deprivation Index (MDSI).[25]

3) Previously dispensed psychotropic medications (i.e., dispensed prior to OUD or the index date)
    a. Anxiolytics
    b. Hypnotics/sedatives
    c. Antipsychotics
    d. Antidepressants
    e. Analgesics (e.g., opioid analgesics)
    f. Medications used in opioid dependence (e.g., methadone, buprenorphine).

5.3.7 Statistical methods

5.3.7.1 Baseline assessment

Differences between cases and controls were explored according to demographics, mental health variables, and previously dispensed psychotropic medications. Odds ratios (ORs) with 95% confidence intervals were calculated for each covariate among cases and controls using a 2x2 table. Chi-square tests were carried out to examine differences between cases and controls for dichotomous data at baseline, and independent sample t-tests were carried out for continuous data. A Pearson R value of ≥ 0.80 was used to demonstrate multi-collinearity between exposure

variables.[26] Material and social deprivation indices were recoded and analyzed as continuous variables.

5.3.7.2 Data analysis

Conditional logistic regression analysis was used to calculate adjusted odds ratios (aORs) with 95% confidence intervals for measuring the strength of the association between the outcome and exposure variables. We used $P \leq 0.05$ (two-tailed) to determine statistical significance. A "full" model building approach, inclusive of statistically and clinically significant covariates, were used to carry out the analysis. Any missing data were imputed using the mean value. IBM SPSS (version 28) was used to perform the statistical analysis.

5.3.7.3 Post-hoc analyses

Additional analyses were conducted exploring whether the following pre-existing comorbidities were associated with subsequent OUD: 1) anxiety and depressive disorders, 2) anxiety disorders and alcohol–related disorders, 3) depressive disorder and alcohol use disorders, 4) anxiety, depressive and alcohol-related disorders. To account for testing multiple hypotheses, we adjusted the significance level to $P \leq 0.01$.[27]

5.4 RESULTS

We identified 1,852 emerging adults with OUD (cases) and 7,392 age/sex-matched emerging adults without OUD (controls). **FIGURE 1** displays the study flow chart.

5.4.1 Baseline characteristics

TABLE 1 shows the baseline characteristics. The mean age of the cases was 22.6 (SD=1.98) years at baseline, 53.2% were male, 82.3% resided in an urban residence, 48.5% were categorized in the third intermediate or highest social deprivation category, and 45.4% were categorized in the third intermediate or highest material deprivation category. At any point during the study period (irrespective of OUD diagnosis), 85.1% of the cases had a record of an anxiety disorder, 47.9% had a record of a depressive disorder, and 46.7% had a record of an alcohol-related disorder. Among cases, incident diagnosis of OUD occurred at a mean age of 20.3 (SD=2.41) years, followed by substance-related disorders at 18.8 (SD=2.83) years, alcohol-related disorders at 18.8

(SD=2.90) years, depressive disorders at 17.9 (SD=3.50) years, and anxiety disorders at 16.2 (SD=4.33) years.

Cases were more likely than controls to have a diagnosis of one or more of the following mental health disorders at any point during the study period (i.e., before or after incident OUD diagnosis): anxiety disorder, OR=9.13 (95% CI, 7.97 – 10.5), depressive disorder, OR=10.1 (95% CI, 8.94 – 11.4), alcohol-related disorder, OR=19.05 (95% CI, 16.5 – 22.0). Cases were more likely than controls to be dispensed the following psychotropic medications at any point during the study period (i.e., before or after incident OUD diagnosis): anxiolytics, OR=7.29 (95% CI, 6.51 – 8.16), antidepressants, OR=8.78 (95% CI, 7.82 – 9.86), opioid analgesics, OR=2.51 (95% CI, 2.26 – 2.80), antipsychotics, OR=13.5 (95% CI, 11.9 – 15.4), hypnotics/sedatives, OR=7.65 (95% CI, 6.66 – 8.79), and medications for opioid dependence, OR=1,630 (95% CI, 524 – 5,075). Cases were also more likely than controls to be at risk for social deprivation ($p<0.001$), and material deprivation ($p<0.001$). Moreover, 736 cases (39.8%) were dispensed a medication for opioid dependence, compared to three controls (0.04%) were prescribed a medication for opioid dependence.

5.4.2 Main findings

TABLE 2 shows the main findings. After controlling for additional covariates, we found that pre-existing anxiety disorders were associated with OUD, aOR=2.53 (95% CI, 2.16 – 2.96), pre-existing depressive disorders were associated with OUD, aOR=2.20 (95% CI, 1.80 – 2.70), and pre-existing concurrent anxiety and depressive disorders were associated with OUD, aOR=1.94 (95% CI, 1.81 – 2.40).

5.4.2.1 Exploratory post-hoc analyses

Post-hoc analyses revealed that concurrent pre-existing anxiety and alcohol-related disorders were associated with OUD, aOR=5.22 (95% CI, 4.03 – 6.77), concurrent preexisting depression and alcohol-related disorder was associated with OUD, aOR=6.47 (95% CI, 4.73 – 8.84), concurrent preexisting anxiety, depression and alcohol-related disorder was associated with OUD, aOR=6.09 (95% CI, 4.41 – 8.42). **S3** shows the SPSS output of each regression model.

5.5 INTERPRETATION

To our knowledge, this is the first study to examine whether preexisting anxiety and depressive disorders were associated with subsequent OUD diagnoses in emerging adults. Our data suggests that a previous diagnosis of either anxiety and/or depressive disorder (e.g., during adolescence) substantially increases the odds of being diagnosed with OUD later on. Additionally, both anxiety and depressive disorders most commonly onset during adolescence, substantially prior to incident OUD diagnoses. This finding provides additional evidence of a temporal relationship suggesting anxiety and/or depressive disorders during adolescence considerably increase the risk of incident OUD during emerging adulthood. However, we did not observe an additive risk of OUD when emerging adults were previously diagnosed with both anxiety and depressive disorders. This finding was contrary to our expectations but may be partially explained by the biological and symptomatic similarities between anxiety and depression.[28,29]

During post-hoc analyses, we observed that a record of an alcohol-related disorder in addition to an anxiety and/or depressive disorder posed an additive/synergistic risk of incident OUD. This finding is novel and may have timely public health policy implications. Moreover, the odds of being diagnosed with an OUD in this scenario is substantially greater than what we observed in either pre-existing anxiety and/or depressive disorders. These results are concordant with recent data obtained from toxicology reports in Alberta, showing 80-82% of all opioid-related deaths involve the use of one or more additional substances such as alcohol, methamphetamine, cocaine or benzodiazepines.[30,31] Concurrent use of sedatives such as alcohol and benzodiazepines increase risk of respiratory depression and death, particularly when used in conjunction with opioids.[32,33] Evidence suggests over half of adults with OUD use alcohol concurrently with opioids.[33]

Our findings contribute knowledge to previous research.[34,35] In particular, a case-control study from Ontario, Canada (2015) found that dispensed benzodiazepines were associated with an increased risk of opioid-related mortality among adults in methadone maintenance therapy.[34] This study may suggest that these psychotropic medications, and/or the underlying mental health conditions such as anxiety disorders, may be associated with OUD and/or opioid-related mortality. Similarly, we also found evidence that dispensed prescriptions for antidepressants, anxiolytics, antipsychotics, opioid analgesics, or hypnotics/sedatives were temporally associated with OUD in emerging adults, but less so than anxiety, depressive and alcohol-related disorders. We found evidence that these preexisting mental health conditions (and psychotropic medications) posed a

substantially increased odds of incident OUD compared to previously dispensed opioid analgesic prescriptions.

Our findings suggest that mental health disorders of sufficient severity to warrant pharmacotherapy (i.e., moderate/severe) may increase the risk of OUD. This was evidenced by the observation that each class of previously dispensed psychotropic medications were associated with an increased odds of OUD compared to preexisting anxiety and/or depressive disorders. Another noteworthy finding includes the observation that emerging adults from rural or urban settings may be equally as likely to develop OUD, contrasting with previous research.[36] As a result our findings may be generalizable for emerging adults in both urban and rural communities.

5.5.1 Limitations

Some unavoidable limitations warrant cautious interpretations of the findings. First, research based on administrative data is inherently limited by the accuracy of the diagnostic data recorded.[37] The reliability of the OUD case definition cannot be guaranteed; however, we observed a statistically significant difference between cases and controls on dispensed medication for opioid dependence, suggesting accurate case/control definitions. We were unable to obtain data on the severity of anxiety or depression, precluding the ability to observe a dose-response gradient. However, we can infer from the pharmaceutical data that a prescription of an anxiolytic or antidepressant implies severity of illness warranting treatment.

Individuals diagnosed with OUD prior to 2007 were excluded since pertinent pharmaceutical data were not accessible prior to April 1, 2008. Only four eligible cases were excluded due to this restriction, suggesting that this decision had a negligible impact on our results. The pharmaceutical data we obtained suggest that other underlying chronic conditions, such as chronic pain, bipolar disorder, or schizophrenia, may also play role in the pathogenesis of OUD for some emerging adults. However, these specific diagnoses were not collected in our study as these were not based on our *a priori* study hypotheses. Our findings suggest multiple pathways for the etiology of OUD may remain beyond the diagnoses of anxiety, depressive and alcohol-related disorders, but these disorders, in particular, warrant further examination.

5.5.2 Conclusions

Our findings suggest that adolescents and emerging adults diagnosed with anxiety and/or depressive disorders may be at substantial risk of developing an OUD. Evidence suggests the addition of a concurrent alcohol-related disorder considerably amplifies this risk. Clinicians treating adolescents and emerging adults with mental health concerns should consider proactively screening for substance and/or alcohol use using brief interventions.[38] Evidence-informed and non-judgmental discussions regarding education and risk mitigation should also be considered.[39,40] Increased awareness and research regarding the potential impact of alcohol use among adolescents and emerging adults with anxiety and depressive disorders is recommended.

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5.7 ADDITIONAL INFORMATION

5.7.1 Funding

This research has been funded by the generous support of the Stollery Children's Hospital Foundation through the Women and Children's Health Research Institute.

5.7.2 Role of the funder

The funding source had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

5.7.3 Data sharing statement

The original patient dataset is held at Alberta Health Services and may be released if eligibility criteria are met.

5.7.4 Conflict of interest statement

None reported.

5.7.5 Author contributions

TM, KO and RL had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. TM, RL, KO, SV developed the research questions and methods. TM produced the initial draft of the manuscript. AA, XL assisted in refinement of the research questions, methods, interpretation and revisions of the manuscript. EY extracted, cleaned the data and provided substantial revisions to the methods and manuscript. All authors have contributed substantially to the conception, acquisition, analysis, interpretation of data, and have approved the final version of this manuscript.

5.7.6 Acknowledgements

We would like to thank the staff at Alberta Health and Alberta Health Services for their assistance in obtaining the dataset.

5.8 TABLES

5.8.1 TABLE 1. Baseline characteristics of cases and controls

Variable	**Cases (N=1,848)**	**Controls (N=7,392)**	**p value**
Demographic characteristics			
Age, years (mean ± SD)*	22.6 ± 1.98	22.6 ± 1.98	
Age, years No. (%)			
18	59 (3.19)	236 (3.19)	
19	94 (5.09)	376 (5.09)	
20	167 (9.04)	668 (9.04)	
21	216 (11.7)	864 (11.7)	
22	237 (12.8)	948 (12.8)	
23	333 (18.0)	1332 (18.0)	
24	350 (18.9)	1400 (18.9)	
25	392 (21.2)	1568 (21.2)	
Gender*			
Male N (%)	983 (53.2)	3932 (53.2)	
Location of residence			
Urban N (%)	1520 (82.3)	6124 (82.8)	0.545
Socioeconomic status			

Material deprivation index quintile N (%)			<0.001
1 (Least deprived)	260 (14.1)	1229 (16.6)	
2	315 (17.0)	1368 (18.5)	
3	325 (17.6)	1309 (17.7)	
4	351 (19.0)	1531 (20.1)	
5 (Most deprived)	488 (26.4)	1618 (21.9)	
Missing	109 (5.90)	337 (4.56)	
Social deprivation index quintile N (%)			<0.001
1 (Least deprived)	228 (12.3)	1499 (20.3)	
2	262 (14.2)	1284 (17.4)	
3	353 (19.1)	1344 (18.2)	
4	395 (21.4)	1558 (21.1)	
5 (Most deprived)	501 (27.1)	1370 (18.5)	
Missing	109 (5.90)	337 (4.56)	
Mental health disorders N (%)			
Anxiety disorders	1572 (85.1)	2839 (38.4)	<0.001
Preexisting anxiety disorders	1343 (72.7)	2247 (30.4)	<0.001

Depressive disorders	885 (47.9)	616 (8.33)	<0.001
Preexisting depressive disorders	641 (34.7)	463 (6.26)	<0.001
Anxiety and depressive disorders	849 (45.9)	546 (7.39)	<0.001
Preexisting anxiety and depressive disorder	587 (31.8)	403 (5.45)	<0.001
Substance use disorders	1820 (98.5)	417 (5.60)	<0.001
Preexisting substance use disorders	1169 (62.3)	283 (5.45)	<0.001
Alcohol-related disorders	863 (46.7)	325 (4.40)	<0.001
Preexisting alcohol use disorders	537 (29.1)	222 (3.00)	<0.001
Anxiety and alcohol-related disorders	798 (43.2)	242 (3.27)	<0.001
Preexisting anxiety and alcohol-related disorders	467 (25.3)	149 (2.02)	<0.001
Depressive and alcohol-related disorders	573 (31.0)	128 (1.73)	<0.001
Depressive and alcohol-related disorders	317 (17.2)	80 (1.08)	<0.001
Anxiety, depressive and alcohol-related disorders	552 (28.2)	120 (1.62)	<0.001

Preexisting anxiety depressive and alcohol-related disorders	299 (16.2)	73 (0.99)	<0.001
Record of dispensed medications N (%)			
Anxiolytics	991 (53.6)	1012 (13.7)	<0.001
Preexisting anxiolytics	672 (36.4)	660 (8.93)	<0.001
Antidepressants	1342 (72.6)	1715 (23.2)	<0.001
Preexisting antidepressants	968 (52.4)	1203 (16.3)	<0.001
Opioid analgesics	1263 (68.3)	3416 (46.2)	<0.001
Preexisting opioid analgesics	1018 (55.1)	2589 (35.0)	<0.001
Antipsychotics	932 (50.04)	517 (6.99)	<0.001
Preexisting antipsychotics	566 (30.6)	369 (4.99)	<0.001
Hypnotics/sedatives	558 (30.2)	425 (5.75)	<0.001
Preexisting hypnotics/sedatives	387 (20.9)	275 (3.72)	<0.001
Medications for opioid dependence	736 (39.8)	3 (0.04)	<0.001
Preexisting medications for opioid dependence	121 (6.55)	0	

Age of incident diagnosis, mean years (+/- SD)			
OUD	20.3 (2.41)		
Substance-related disorder	18.8 (2.83)	18.7 (3.16)	0.35
Alcohol-related disorder	18.8 (2.90)	18.7 (2.94)	0.74
Depressive disorder	17.9 (3.50)	17.6 (3.51)	0.12
Anxiety disorder	16.2 (4.33)	16.4 (4.58)	0.45

Footnotes: "preexisting" implies that the initial administrative record of diagnosis or medication dispensing was recorded and dated prior to the incident diagnosis date of OUD or the corresponding index date in the controls. * implies cases and controls were matched on this variable.

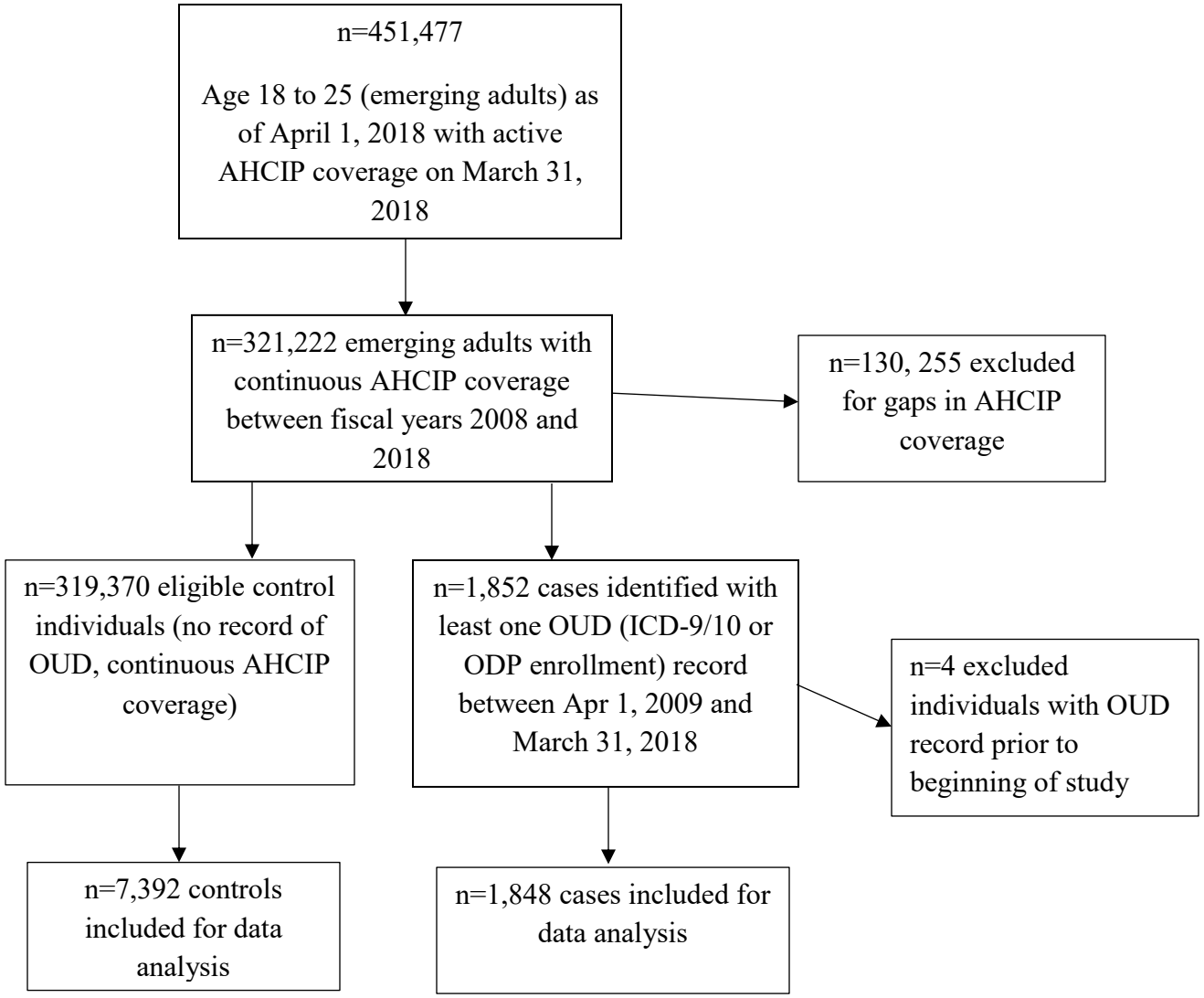
5.8.2 TABLE 2. Main findings

Exposure category	**Study participants, N (%)**		**OR (95% CI)**	
	Cases	**Controls**	**Unadjusted**	**Adjusted**
	1,848	7,392		
Exposure prior to OUD or index date				
Mental health diagnoses				
Anxiety disorders	1,343 (72.7)	2,247 (30.4)	6.09 (5.44 – 6.82)	2.53 (2.16 – 2.96)
Depressive disorders	641 (34.7)	463 (6.26)	7.95 (6.95 – 9.09)	2.20 (1.80 – 2.70)
Anxiety and depressive disorders*	587 (31.8)	403 (5.45)	8.07 (7.02 – 9.29)	1.94 (1.56 – 2.40)
Anxiety and alcohol-related disorders*	467 (25.3)	149 (2.01)	16.4 (13.6 – 19.9)	6.68 (5.20 – 8.59)
Depressive and alcohol-related disorders*	317 (17.2)	80 (1.08)	18.9 (14.7 – 24.3)	6.47 (4.73 – 8.84)
Anxiety, depressive and alcohol-related disorders*	299 (16.2)	73 (0.99)	19.4 (14.9 – 25.1)	6.09 (4.41 – 8.42)

Footnotes: *indicates both conditions were diagnosed in an individual prior to the OUD diagnosis or corresponding index date in controls.

5.9 FIGURES

5.9.1 FIGURE 1. Study flow chart



5.10 SUPPLEMENTARY FILES

5.9.1 Supplementary File 1. Eligibility criteria for OUD case definition

A minimum of one the following criteria was required for OUD diagnosis (case inclusion):

1. A physician billing claim record with one or more ICD-9 diagnosis codes 304.0, 305.5 or 304.7 in any of 3 diagnosis code fields
2. An ambulatory record with one or more ICD-10 diagnosis codes F11.1 or F11.2 in any of 10 diagnosis code fields
3. An inpatient record with one or more ICD-10 diagnosis codes F11.1 or F11.2 in any of 10 diagnosis code fields
4. An admission to an Alberta Health Services Opioid Dependency Program

5.10.2 Supplementary File 2. List of ATC codes

Field	Description/definition	Data source
Rx_Opioid_pre	Drug dispensed for opioid dependence at any point prior to OUD diagnosis, defined by ATC code N07BC. Note that PIN data starts in April 2008.	PIN
Rx_Opioid_post	Drug dispensed for opioid dependence at any point after OUD diagnosis, defined by ATC code N07BC. Note that PIN data starts in April 2008.	PIN
rx_Anxiolytic_pre	Drug dispensed for anxiety at any point prior to OUD diagnosis, defined by ATC code N05B. Note that PIN data starts in April 2008.	PIN
rx_Anxiolytic_post	Drug dispensed for anxiety at any point after OUD diagnosis, defined by ATC code N05B. Note that PIN data starts in April 2008.	PIN
Rx_hypnotic_pre	Drug dispensed for hypnotics/sedatives at any point prior to OUD diagnosis, defined by ATC code N05CD, N05CF, N05CA, N05CB. Note that PIN data starts in April 2008.	PIN
Rx_hypnotic_post	Drug dispensed for hypnotics/sedatives at any point after OUD diagnosis, defined by ATC code N05CD, N05CF, N05CA, N05CB. Note that PIN data starts in April 2008.	PIN
Rx_antipsych_pre	Drug dispensed for Antipsychotics at any point prior to OUD diagnosis, defined by ATC code N05A. Note that PIN data starts in April 2008.	PIN
Rx_antipsych_post	Drug dispensed for Antipsychotics at any point after OUD diagnosis, defined by ATC code N05A. Note that PIN data starts in April 2008.	PIN

Rx_antidep_pre	Drug dispensed for Antidepressants at any point prior to OUD diagnosis, defined by ATC code N06A. Note that PIN data starts in April 2008.	PIN
Rx_antidep_post	Drug dispensed for Antidepressants at any point after OUD diagnosis, defined by ATC code N06A. Note that PIN data starts in April 2008.	PIN
Rx_analgesic_pre	Drug dispensed for Opioid analgesic at any point prior to OUD diagnosis, defined by ATC code N02A. Note that PIN data starts in April 2008.	PIN
Rx_analgesic_post	Drug dispensed for Opioid analgesic at any point after OUD diagnosis, defined by ATC code N02A. Note that PIN data starts in April 2008.	PIN

Footnotes: Abbreviations: DAD = Discharge Abstract Database; NACRS = National Ambulatory Care Reporting System; AACRS = Alberta Ambulatory Care Reporting System; CLM = Practitioner Claims; PIN = Pharmaceutical Information Network; REG = Provincial Registry; PAMP = Pampalon Deprivation Index; ODP = Opioid Dependency Program

5.10.3 Supplementary File 3. SPSS output of conditional logistic regression analyses

Model 1 – pre-existing anxiety

```
GET
  FILE='\\nurs.ualberta.ca\HRDR\TylerMarshall\Thesis\Chap 2 Case
Control\Analysis\Case Control Master File Dec 2 2020.sav'.
DATASET NAME DataSet1 WINDOW=FRONT.
COXREG case_control_time
  /STATUS=Outcome(1)
  /STRATA=strata_group
  /METHOD=ENTER anxiety_pre alcohol_pre rx_Anxiolytic_pre rx_hypnotic_pre
rx_antipsych_pre
    rx_antidep_pre rx_analgesic_pre QUINTMAT QUINTSOC
  /PRINT=CI(95)
  /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).
```

Cox Regression

Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	1739	18.8%
	Censored	6638	71.8%
	Total	8377	90.7%
Cases dropped	Cases with missing values	446	4.8%
	Cases with negative time	0	0.0%
	Censored cases before the earliest event in a stratum	417	4.5%
	Total	863	9.3%
Total		9240	100.0%

a. Dependent Variable: Dummy

Block 0: Beginning Block

Omnibus Tests of Model Coefficients

-2 Log Likelihood
5452.395

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]

	Overall (score)			Change From Previous Step			Change From Previous Block		
-2 Log Likelihood	Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
3389.418	2202.099	9	.000	2062.977	9	.000	2062.977	9	.000

a. Beginning Block Number 1. Method = Enter

Variables in the Equation

							95.0% CI for Exp(B)	
	B	SE	Wald	df	Sig.	Exp(B)	Lower	Upper
Pre-existing anxiety	.929	.080	133.611	1	.000	2.532	2.163	2.963
Pre-existing alcohol use disorder	1.805	.114	250.154	1	.000	6.081	4.862	7.605
Pre-existing anxiolytic	.781	.093	70.237	1	.000	2.184	1.819	2.622
Pre-existing hypnotic sedative	.857	.127	45.426	1	.000	2.357	1.837	3.024
Pre-existing antipsychotic	.721	.107	45.668	1	.000	2.056	1.668	2.534

Pre-existing anti depressants	.552	.089	38.193	1	.000	1.736	1.458	2.068
Pre existing opioid analgesic	.561	.073	58.754	1	.000	1.752	1.518	2.022
Material deprivation	.051	.024	4.420	1	.036	1.053	1.003	1.104
Social deprivation	.165	.025	45.140	1	.000	1.179	1.124	1.237

Model 2 – Pre-existing depression

```
COXREG case_control_time
  /STATUS=Outcome(1)
  /STRATA=strata_group
  /METHOD=ENTER depression_pre alcohol_pre rx_Anxiolytic_pre rx_hypnotic_pre rx_antipsych_pre
    rx_antidep_pre rx_analgesic_pre QUINTMAT QUINTSOC
  /PRINT=CI(95)
  /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).
```

Cox Regression

Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	1739	18.8%
	Censored	6638	71.8%
	Total	8377	90.7%
Cases dropped	Cases with missing values	446	4.8%
	Cases with negative time	0	0.0%

	Censored cases before the earliest event in a stratum	417	4.5%
	Total	863	9.3%
Total		9240	100.0%

a. Dependent Variable: Dummy

Block 0: Beginning Block

Omnibus Tests of Model Coefficients

-2 Log Likelihood
5452.395

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]

	Overall (score)			Change From Previous Step			Change From Previous Block		
-2 Log Likelihood	Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
3465.438	2171.825	9	.000	1986.957	9	.000	1986.957	9	.000

a. Beginning Block Number 1. Method = Enter

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
Pre-existing depression	.789	.103	58.696	1	.000	2.202	1.799	2.695
Pre-existing alcohol use disorder	1.747	.116	225.224	1	.000	5.740	4.569	7.211
Pre-existing anxiolytic	.921	.092	99.228	1	.000	2.512	2.095	3.011
Pre-existing hypnotic sedative	.950	.128	54.661	1	.000	2.586	2.010	3.326
Pre-existing antipsychotic	.722	.109	43.693	1	.000	2.058	1.662	2.549
Pre-existing anti depressants	.722	.087	68.217	1	.000	2.059	1.735	2.444
Pre existing opioid analgesic	.582	.072	64.403	1	.000	1.789	1.552	2.062
Material deprivation	.057	.024	5.523	1	.019	1.059	1.009	1.110
Social deprivation	.166	.024	46.679	1	.000	1.181	1.126	1.239

Model 3 – pre-existing depression and anxiety

```
COXREG case_control_time
  /STATUS=Outcome(1)
  /STRATA=strata_group
  /METHOD=ENTER Anx_Dep_Pre alcohol_pre rx_Anxiolytic_pre rx_hypnotic_pre rx_antipsych_pre
    rx_antidep_pre rx_analgesic_pre QUINTMAT QUINTSOC
  /PRINT=CI(95)
  /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).
```

Cox Regression

Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	1739	18.8%
	Censored	6638	71.8%
	Total	8377	90.7%
Cases dropped	Cases with missing values	446	4.8%
	Cases with negative time	0	0.0%
	Censored cases before the earliest event in a stratum	417	4.5%
	Total	863	9.3%
Total		9240	100.0%

a. Dependent Variable: Dummy

Block 0: Beginning Block

Omnibus Tests of Model Coefficients

-2 Log Likelihood
5452.395

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]

	Overall (score)			Change From Previous Step			Change From Previous Block		
-2 Log Likelihood	Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
3487.222	2149.447	9	.000	1965.173	9	.000	1965.173	9	.000

a. Beginning Block Number 1. Method = Enter

Variables in the Equation

							95.0% CI for Exp(B)	
	B	SE	Wald	df	Sig.	Exp(B)	Lower	Upper
Pre-existing anxiety and depression	.660	.109	36.669	1	.000	1.936	1.563	2.397
Pre-existing alcohol use disorder	1.797	.116	240.771	1	.000	6.032	4.807	7.569
Pre-existing anxiolytic	.916	.092	98.489	1	.000	2.500	2.086	2.996
Pre-existing hypnotic sedative	.926	.128	52.413	1	.000	2.523	1.964	3.242
Pre-existing antipsychotic	.752	.110	47.066	1	.000	2.120	1.711	2.628
Pre-existing anti depressants	.762	.087	76.606	1	.000	2.142	1.806	2.540
Pre existing opioid analgesic	.577	.072	63.916	1	.000	1.781	1.546	2.052
Material deprivation	.056	.024	5.315	1	.021	1.057	1.008	1.109
Social deprivation	.167	.024	47.539	1	.000	1.182	1.127	1.240

Model 4 – pre-existing anxiety and alcohol use disorder

Block 0: Beginning Block

```
COXREG case_control_time
  /STATUS=Outcome(1)
  /STRATA=strata_group
  /METHOD=ENTER Anx_Alc_Pre2 rx_Anxiolytic_pre rx_hypnotic_pre rx_antipsych_pre rx_antidep_pre
    rx_analgesic_pre QUINTMAT QUINTSOC
  /PRINT=CI(95)
  /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).
```

Cox Regression

Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	1739	18.8%
	Censored	6638	71.8%
	Total	8377	90.7%
Cases dropped	Cases with missing values	446	4.8%
	Cases with negative time	0	0.0%
	Censored cases before the earliest event in a stratum	417	4.5%
	Total	863	9.3%
Total		9240	100.0%

a. Dependent Variable: Dummy

Block 0: Beginning Block

Omnibus Tests of Model Coefficients

-2 Log Likelihood
5452.395

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]

	Overall (score)			Change From Previous Step			Change From Previous Block		
-2 Log Likelihood	Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
3604.450	2031.113	8	.000	1847.945	8	.000	1847.945	8	.000

a. Beginning Block Number 1. Method = Enter

Variables in the Equation

							95.0% CI for Exp(B)	
	B	SE	Wald	df	Sig.	Exp(B)	Lower	Upper
Pre-existing anxiety and alcohol	1.899	.128	219.745	1	.000	6.682	5.198	8.590
Pre-existing anxiolytic	.904	.091	98.895	1	.000	2.469	2.066	2.950
Pre-existing hypnotic sedative	.897	.125	51.398	1	.000	2.453	1.919	3.135
Pre-existing antipsychotic	.923	.105	77.392	1	.000	2.516	2.048	3.090
Pre-existing anti depressants	.874	.083	109.999	1	.000	2.396	2.035	2.821
Pre existing opioid analgesic	.585	.071	67.929	1	.000	1.795	1.562	2.063

Material deprivation	.056	.024	5.523	1	.019	1.058	1.009	1.108
Social deprivation	.175	.024	53.280	1	.000	1.191	1.136	1.248

Model 5 – pre-existing depression and alcohol use disorder

```
COXREG case_control_time
  /STATUS=Outcome(1)
  /STRATA=strata_group
  /METHOD=ENTER Dep_Alc_Pre2 rx_Anxiolytic_pre rx_hypnotic_pre rx_antipsych_pre rx_antidep_pre
    rx_analgesic_pre QUINTMAT QUINTSOC
  /PRINT=CI(95)
  /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).
```

Cox Regression

Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	1739	18.8%
	Censored	6638	71.8%
	Total	8377	90.7%
Cases dropped	Cases with missing values	446	4.8%
	Cases with negative time	0	0.0%
	Censored cases before the earliest event in a stratum	417	4.5%
	Total	863	9.3%
Total		9240	100.0%

a. Dependent Variable: Dummy

Block 0: Beginning Block

Omnibus Tests of Model Coefficients

-2 Log Likelihood
5452.395

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]

	Overall (score)			Change From Previous Step			Change From Previous Block		
-2 Log Likelihood	Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
3700.309	1920.902	8	.000	1752.086	8	.000	1752.086	8	.000

a. Beginning Block Number 1. Method = Enter

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
Pre-existing depression and alcohol	1.867	.159	137.135	1	.000	6.466	4.731	8.838
Pre-existing anxiolytic	.975	.089	120.884	1	.000	2.652	2.229	3.155

Pre-existing hypnotic sedative	.902	.122	54.755	1	.000	2.465	1.941	3.130
Pre-existing antipsychotic	.937	.103	82.414	1	.000	2.553	2.085	3.125
Pre-existing anti depressants	.897	.081	121.706	1	.000	2.453	2.091	2.876
Pre existing opioid analgesic	.601	.070	73.568	1	.000	1.823	1.589	2.091
Material deprivation	.064	.023	7.405	1	.007	1.066	1.018	1.116
Social deprivation	.174	.024	54.399	1	.000	1.190	1.136	1.246

Model 6 Pre-existing anxiety, depression and alcohol use disorder

```
COXREG case_control_time
  /STATUS=Outcome(1)
  /STRATA=strata_group
  /METHOD=ENTER anx_dep_alc_pre2 rx_Anxiolytic_pre rx_hypnotic_pre rx_antipsych_pre rx_antidep_pre
    rx_analgesic_pre QUINTMAT QUINTSOC
  /PRINT=CI(95)
  /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).
```

Cox Regression

Case Processing Summary

		N	Percent
Cases available in analysis	Event[a]	1739	18.8%
	Censored	6638	71.8%
	Total	8377	90.7%
Cases dropped	Cases with missing values	446	4.8%

	Cases with negative time	0	0.0%
	Censored cases before the earliest event in a stratum	417	4.5%
	Total	863	9.3%
Total		9240	100.0%

a. Dependent Variable: Dummy

Block 0: Beginning Block

Omnibus Tests of Model Coefficients

-2 Log Likelihood
5452.395

Block 1: Method = Enter

Omnibus Tests of Model Coefficients[a]

	Overall (score)			Change From Previous Step			Change From Previous Block		
-2 Log Likelihood	Chi-square	df	Sig.	Chi-square	df	Sig.	Chi-square	df	Sig.
3721.285	1897.429	8	.000	1731.110	8	.000	1731.110	8	.000

a. Beginning Block Number 1. Method = Enter

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
Pre-existing anxiety depression and alcohol	1.807	.165	119.755	1	.000	6.093	4.408	8.422
Pre-existing anxiolytic	.976	.089	121.343	1	.000	2.653	2.230	3.156
Pre-existing hypnotic sedative	.893	.121	54.155	1	.000	2.442	1.925	3.098
Pre-existing antipsychotic	.947	.103	84.482	1	.000	2.578	2.107	3.155
Pre-existing anti depressants	.906	.081	124.860	1	.000	2.475	2.111	2.901
Pre existing opioid analgesic	.597	.070	73.064	1	.000	1.817	1.584	2.084
Material deprivation	.064	.023	7.448	1	.006	1.066	1.018	1.116
Social deprivation	.175	.024	55.215	1	.000	1.191	1.137	1.247

CHAPTER 6: CONCLUSION

6.1 Background

Three quarters of mental illnesses commence before age 25[1], with anxiety and depression among the most prevalent.[2-4] Promising research[5-8] around person-centred care and shared decision-making (SDM) among adult patients with chronic diseases has inspired investigations into whether SDM may be useful among special populations such as emerging adults (e.g., individuals 18-29 years). In this dissertation, we sought to: i) explore the relationship between SDM and clinically relevant outcomes such as patient health engagement (PHE), health-related quality of life (HRQL), and symptoms of anxiety and/or depression in emerging adults; ii) develop a deeper understanding of the lived experience of emerging adults with anxiety and/or depression, including how these individuals prefer to make mental health decisions; and, iii) to investigate whether previously diagnosed anxiety and/or depressive disorders are temporally associated with incident opioid use disorder (OUD) among emerging adults.

6.2 Summary of findings

In chapter 2, a systematic review was conducted exploring five health databases for prospectively controlled trials using SDM in the treatment of anxiety and/or depressive disorders in adults (18-64 years). We aimed to analyze any studies of emerging adults separately. Six RCTs[9-14] were identified that met our *a priori* inclusion criteria. All included studies involved adult patients, ranging 18-64 years, with various depressive disorders. No studies were found that investigated the impact of SDM in patients diagnosed with anxiety disorders.[12] The data suggested that SDM may be most likely to improve the following outcomes: i) patient satisfaction with care, ii) involvement in decision-making, ii), and iii) receiving adequate treatment (e.g., selective serotonin re-uptake inhibitors) for depression. One study found that SDM was linked to a decrease in symptoms of anxiety among people with depression.[12]

We hypothesized that if SDM enhances outcomes such as increasing the probability of obtaining adequate treatment (e.g., reducing concerns around pharmacotherapy, appropriate medication selection and/or dose of medication), knowledge gain, and increased treatment adherence, then health outcomes such as relapse rates, HRQL, and health system utilization/costs might improve

downstream. For instance, evidence suggests that improvements in treatment adherence are strongly associated with improved mental health outcomes.[15,16]

Our findings were consistent with previous systematic reviews from other patient populations[17,18] suggesting SDM may be a promising approach for improving patient-reported outcomes such as: i) patient satisfaction with care, ii) knowledge gain, iii) decisional comfort, and treatment-related outcomes such as: i) adequate treatment selection, particularly when a collaborative care (e.g., team-based approach to care) model is used adjunctively with SDM. No research was found exploring the use of SDM in emerging adults with anxiety and/or depression, warranting future exploration. Future research is also warranted among people with anxiety disorders as we obtained novel, but limited, evidence that SDM may be beneficial in this population.

In chapter 3, we conducted a qualitative study among twelve emerging adults who sought treatment for anxiety and/or depression in three outpatient (two mental health, one primary care) and one inpatient settings in Alberta. Using an inductive/exploratory approach guided by narrative inquiry, we explored the life stories and lived experience of emerging adults and talked with them about how they made decisions around their mental health concerns. Using this approach, we learned more about the unique characteristics, stories and lived experiences of each participant. For instance, some participants discussed having stable home lives, while others reported a more stressful home life. Some individuals reported feeling stressed in relation to academics during high school, while others were more concerned with social acceptance or "fitting in." Participants had a variety of ideas about the meaning of "recovery" or "getting back on my feet." These meanings include: a desired to return to work, hopes to attend university without feeling anxious, a desire to not be judged by their peers, and improvements in their sleep and energy levels.

We also identified several similarities. For example, social or family support (specifically a trusted, non-judgmental individual) was often a facilitator for seeking professional mental health services, and all participants discussed a strong desire for developing autonomy/independence They were also sensitive to perceived stigma, judgment and/or paternalistic attitudes. All of the participants showed interest in being more involved in their mental health decision-making although some felt they did not know enough about their diagnosis or mental health condition(s). Another common theme, although not expressed by all participants, included a discussion about various types of avoidant coping behaviours, such as social withdrawal/isolation, often in

conjunction with substance/alcohol use – particularly during times of acute distress. This particular finding was also supported by quantitative evidence obtained from our demographic questionnaire, where we found that seven of twelve participants had reported using drugs and/or alcohol in effort to cope with distress within the last week. In summary, we have added to the evidence base about anxiety and depression in emerging adults by providing initial information about the importance individualized approaches to care, and about more inclusion in treatment planning and decision-making.

In chapter 4, we examined whether SDM was associated with PHE, HRQL, and symptoms of anxiety and/or depression in emerging adults, using cross-sectional approach and data obtained from a separate and overarching pan-provincial study on SDM. Data were obtained from 31 healthcare providers and 42 patients 18-29 years of age. Limited variability in the SDM scores, including no "unacceptable" scores reported by any of the participants, precluded a meaningful analysis of the relationship between SDM and PHE, HRQL, and anxiety and/or depression. We found no difference between "acceptable" and "excellent" score for SDM and PHE. However, we did find that HRQL and anxiety/depression were negatively associated with PHE. Two key points emerge from this study: i) future studies of SDM must address the challenges regarding accurate measurement of SDM (e.g., reducing the ceiling effect), and issues around recruitment and data collection such as selection bias and social desirability response bias, which may have contributed to the ceiling effect; and ii) poor HRQL and clinically significant symptoms of anxiety/depression may impact PHE during a clinic visit. Since this was a small cross-sectional study and no longitudinal data were collected, it is not possible to draw any conclusions about the potential impact of using SDM over time on these outcomes.

In chapter 5, we explored whether previous diagnoses of anxiety and/or depressive disorders were associated with OUD identified/diagnosed during emerging adulthood (defined in this study as 18-25 years on April 1, 2018). Anxiety and/or depressive were selected because these are common psychiatric disorders that emerge during adolescence and/or emerging adulthood. Moreover, it is known that life-threatening substance use disorders such as OUD[19] commonly onset during emerging adulthood.[20] In North America, opioid-related overdoses are a leading cause of preventable death in adults.[19] For this age/sex matched case-control study, we obtained a large sample (n=1,842 cases, n=7,368 controls) of eligible emerging adults (i.e., Alberta residents with

continuous provincial insurance coverage). After controlling for key covariates such as opioid analgesics, we found that preexisting anxiety and/or depressive disorders were independently associated with OUD. However, co-occurrence of anxiety and depressive disorder was not associated with an exacerbated/additive risk of OUD.

Another key finding was the identification of a temporal sequence of incidence diagnoses among key mental health conditions. We recorded incident diagnosis data of the following conditions: anxiety and/or depressive disorders, substance-related disorders, alcohol-related disorders, and OUD. Among cases, we found that anxiety disorders were diagnosed first in our cohort, followed by depressive disorders, then substance-related disorders and alcohol-related disorders. OUD was most often diagnosed last. (See **TABLE 1** in chapter 5 for more information). During post hoc analysis, we found that preexisting alcohol-related disorders showed a striking independent association with OUD. (See **TABLE 2** in chapter 5). We further examined this association and discovered that concurrent anxiety and/or depressive disorders in addition to an alcohol-related disorder posed a substantial additive risk of OUD, suggesting alcohol-related disorders may be important effect modifiers warranting further examination.

In summary, we learned that previous diagnoses of anxiety and/or depressive disorders during adolescence and/or emerging adulthood are temporally associated with incident OUD during emerging adulthood. Crucially, we learned that the risk increased when an alcohol-related disorder coexisted with these preexisting conditions during emerging adulthood or adolescence. Although methodological limitations warrant caution interpretation, these quantitative findings are congruent with the narratives expressed in our qualitative study and match previous observational research from other jurisdictions.[21,22]

6.3 Limitations

6.3.1 Heterogeneity in the literature

Heterogeneity in the definition of the clinical population, intervention and reporting/measurement of outcomes, posed considerable challenges throughout this dissertation. Heterogeneity in the conceptualization and definition of emerging adulthood in the peer-reviewed literature challenges research, policy and practice. For instance, some studies defined emerging adults as individuals aged 18-25 years[31,32], while others were more inclusive of older individuals (e.g., individuals 18-

29 years)[33], while authors of other key articles used the language "young people" to describe individuals 12-24 years.[34] One reason for this heterogeneity may be that the actual age of the individual may be less important than other factors like one's psychological/emotional maturity level, and environmental contextual factors of the individual such as employment, housing or student status.[33] Heterogeneity in outcome reporting in relevant studies poses challenges for conducting a meta-analysis and drawing firm conclusions. For instance, the included collaborative care studies often selected different outcomes (e.g., adequate depression treatment) than trials that studied SDM, therefore precluding any ability to perform comparisons between SDM and collaborate care on clinical outcomes.

6.3.2 Recruitment and sampling biases

Small participant sample sizes impacted three of four studies in this dissertation. Chapter 2 included a few prospective studies (six in total, and no studies of emerging adults), and the studies in chapter 3 and 4 each recruited less than 50 participants, respectively. The results of chapter 3 were limited to those who had sought treatment. In this qualitative study, we attempted to recruit participants who were not actively using conventional mental health services. For example, we attempted to collect data from supervised consumptions services and other harm reduction centres; however, few individuals met our inclusion criteria.

Unintended and potentially unavoidable participant sampling biases may have limited the generalizability of the findings. In particular, the possibility of selection bias among participants cannot be fully excluded. For example, in chapters 3 and 4, individuals (patients and healthcare providers) who were more likely to value an SDM approach may have been more likely to participate in the study, while those who may have preferred a more traditional approach, were perhaps less inclined to participate. Moreover, we were not able to recruit individuals who were mandated to treatment, or those with mental health symptoms who were not seeking mental health services. We attempted to collect data at two harm reduction centres, but few individuals met the inclusion criteria at these locations.

6.3.3 Researcher/interviewer bias

The validity of research can sometimes be limited by implicit biases, which may influence the interpretation of the data.[23-27] The first author of all studies in this dissertation has personal

experience with mental health and substance use, particularly with regard to lived experiences of close friends and family. This can be a strength, but also a weakness if not carefully examined. Several strategies, such as discussions within the research team, and preparation of memos and field notes were undertaken to reduce the impact of these biases. Further attempts to mitigate this included: i) review of the qualitative data by an experienced researcher, ii) obtaining a priori qualitative interviewing training in the form of coursework, iii) having experience with qualitative research on a previous study, and iv) carefully developing interview questions with the help of expert clinical psychologists.

6.3.4 Challenges of measuring SDM

Adequate conceptualization, definition and measurement of SDM was another major challenge faced throughout this dissertation. For example, in chapter 2, only three studies explicitly measured or evaluated SDM using a standardized instrument. One of these studies used an instrument (PICS) that was not validated for measuring SDM. We used the ASK-MI tool in chapter 4, which is a novel instrument for measuring SDM.

In chapter 4, we are unable to compare high-quality SDM (excellent/acceptable) and low quality SDM (unacceptable) because no "low quality" scores were obtained. Therefore, it was not possible to determine whether SDM was associated with clinically relevant outcomes such as PHE, HRQL, and anxiety/depression. Response biases might have inadvertently contributed to the observed ceiling effect on the ASK-MI questionnaires. For instance, 93% of patients rating SDM as "excellent" compared to 76% of healthcare providers suggesting a possible discrepancy in the perception of SDM. Moreover, no healthcare provider or patient in the study rated the SDM as "unacceptable". Previous knowledge of the potential utility of SDM as described in the consent forms and to the healthcare providers, in addition to previous knowledge of the ASK-MI questionnaires, may have encouraged healthcare providers to ensure they performed each SDM question to the best of their ability. Moreover, patients who valued SDM or have a stronger relationship with their healthcare provider may have been more inclined to participate and provide more positive ratings. It is also plausible that SDM ratings were high and variability was low because SDM may already be commonly used/delivered to a high standard in primary care and mental health settings in Alberta. However, future study will be required to clarify these potential alternative hypotheses due to limitations in our data.

6.3.5 Administrative health data

Reliability issues involving administrative health data specifically impacted our investigation in chapter 5. Administrative data is a cost-effective source for large quantities of patient data in a timely manner; however, data reliability issues are common limitation for this approach. For example, not all facilities and physicians report patient health data consistently or accurately, posing concerns for researchers conducting retrospective chart review studies. Moreover, some patients may be prescribed a medication for a particular condition, but may not necessarily have formally been coded with the corresponding diagnosis in the database. In chapter 5, some individuals with specific substance use disorders, such as OUD, may have been diagnosed with "drug dependence" (ICD-9CM 304), which lacks pertinent information in regard to differential diagnoses such as "opioid-type dependence" (ICD-9CM 304.0), or cannabis dependence (ICD-9CM 304.3).

Fortunately, we used several strategies to mitigate these issues. First, we conducted a sensitivity analysis comparing rates of dispensed medications for opioid dependence (e.g., buprenorphine, methadone) among cases compared to controls using data obtained from the pharmaceutical information network. We observed statistically significant differences in the number of prescribed medications for opioid dependence; thus, increasing our confidence that our case definition for OUD was reliable. Second, we considered individuals treated at an Alberta-based Opioid Dependency Program (ODP) as an OUD case despite lacking an ICD-9 or ICD-10 record. All individuals at this facility are treated exclusively for opioid dependency, which is a key symptom of OUD, but ICD diagnoses are not provided. Unfortunately, we were not able to learn how many cases were derived from the ODP data due to confidentiality concerns.

6.3.6 Epistemological limitations

In this dissertation, several methodological approaches (e.g., quantitative, qualitative, systematic review) were used to address a variety of clinically relevant and person-centred research questions in the areas of emerging adults, anxiety and depression, opioid use disorder, and shared decision-making. Chapter 2 attempted to systematically review the literature to investigate whether SDM improves patient outcomes in adults with anxiety and/or depressive disorders. This is an important initial study, and methodological choice, as it sets the stage for the subsequent chapters. If we had

found robust evidence that SDM does indeed improve outcomes in emerging adults with anxiety and depression, then the subsequent chapters would have been affected; and we could recommend that SDM should be adopted in mental health settings treating anxiety/depression in emerging adults. However, we did not find any such. As a result, it became important to obtain data in emerging adults. We chose to obtain cross-sectional data from an ongoing provincial study to embark on a preliminary assessment of the relationship between SDM and patient outcomes. The main limitation is that the cross-sectional design would not have met criteria for inclusion in our systematic review thus yielding no causal evidence in support or against the use of SDM. However, since no prospective studies were found, it is reasonable to start with observational research. Moreover, the systematic review highlighted several issues with regard to heterogeneity in outcome measurement and reporting of SDM.

Our pilot study (chapter 4) may inform future research regarding overcoming challenges for how to recruit, measure and study SDM. Chapter 3, approaches the study of SDM from a different lens of not investigating determination of the effectiveness of SDM, but inquiring around patient lived experience and better understanding whether person-centred approaches like SDM may be valued or desired by our target population. An effective intervention may be irrelevant if patients do not wish or refuse to use it. Although this approach contrasts epistemologically with our other quantitative methods, the knowledge obtained provides important context to the discussion around SDM in emerging adults. Finally, chapter 5 complements the dissertation by examining the potential longitudinal impacts of the primary mental health conditions under investigation in this dissertation – anxiety and depressive disorders. These are common conditions and by understanding their potential deleterious impact, this highlights importance and urgency to the overall field and body of work.

6.4 Recommendations for future research

Several considerations for future research are listed below in response to limitations in this dissertation.

6.4.1 Heterogeneity in the literature

More high-quality clinical research using a consistent definition of SDM is needed to advance the field. Heterogeneity around the definition and measurement of SDM must be addressed for successful future study, including the conduct of any randomized controlled trials, or meta-analyses.[30] Conducting a scoping review mapping the definitions, followed by a Delphi study to develop consensus may help establish a standardized definition for SDM.

6.4.2 Recruitment and sample size

Novel strategies for recruitment of populations who may not use conventional health services, and those who have been mandated to treatment, may be important in future study building upon this work. More qualitative research in the context of mental health for emerging adults should be considered to help identify values/preferences of emerging adults who do not seek professional mental health services. During this endeavor, investigators should aim to develop meaningful and ethical relationship with potentially vulnerable populations. Offering payment for participation is considered standard practice and is often encouraged by experts in this field. Experts suggest that compensation for research participation may facilitate productive relationships, while rewarding individuals for contributing their time and expertise. However, concerns remain that payment may be viewed as form of coercion, a threat to voluntariness and may even potentially increase drug use. (Anderson & McNair, 2018) Two studies found that incentives (cash or gift certificates) did not increase drug use or perceptions of coercion within six months of study completion. (Fry et al., 2006) Random sampling methods may also be explored to address recruitment and sampling biases, potentially improving internal and external validity in quantitative studies. Additionally, we recommend using a more inclusive age range of 18-29 years (as in chapter 4) as an effective way to improve sample size in future research in emerging adult populations.

6.4.3 Researcher/interviewer bias

Future research should ensure research reflexivity exercises are iterative during each stage of all study types, whether qualitative for quantitative. This is important for identifying pre-existing beliefs or values that may impact the design, conduct and interpretation of the results. Having a multidisciplinary team, with diverse backgrounds, skills and training may also be useful for mitigating researcher biases. Furthermore, it is important for data analysis (coding, extraction,

statistical analysis) to be conducted independently to enhance rigor and to minimize chances for error.

6.4.4 Challenges of measuring SDM

It is plausible that the full impact of SDM may not be realized until several clinic visits have been made, as it may take time to develop a therapeutic relationship. For instance, if the use of SDM over time collectively impacts outcomes such as patient satisfaction, treatment adherence, and adequate treatment, then it would be reasonable to expect that health outcomes may improve over time as well. Longitudinal studies using SDM over several periods and measuring outcomes over several time points may be beneficial in future study.

Accurately measuring SDM was a major challenge for our research and may pose challenges in future research. In chapter 4, a ceiling effect was observed with the ASK-MI data and no "unacceptable" SDM scores were obtained. The ceiling effect observed on SDM scores demonstrates a clear challenge for future studies, and for any controlled studies in particular. To have an adequate control condition, a clear/measurable difference must be established between the intervention and control groups (e.g., treatment vs. placebo). While conducting this research, we learned that achieving this may be more difficult than previously thought. More research is needed to reduce the ceiling effect and to be able to derive more variability in scores required to create dichotomous groups (e.g., high vs. low SDM).

Minor revisions to the ASK-MI tool may be warranted in future study, including the use of language such as "low", "moderate" "complete" SDM to evaluate whether SDM occurred, and to what extent, rather than its acceptability. Although participants were told that their answers were confidential and that healthcare providers receive no punishment or compensation for any of the data collected, more work may need to be done to help conceal the SDM intervention and reduce the potential for performance bias. Adapting the ASK-MI instrument for an observer rated version could be considered so that treatment sessions could be video recorded, and the SDM could be rated independently by an observer, reducing the risk of participant response bias. Care would need to be taken to ensure that the sessions remained anonymous and confidential to protect both the healthcare provider and patient.

We suggest measuring SDM using validated tools such as the ASK-MI[35] or OPTION[36,37] tools, and mental health symptoms by using validated tools such as the Hospital Anxiety and Depression Scale (HADS).[38] In future studies of emerging adults with anxiety and depression, the use of the core outcome set for anxiety and depression should be considered.[39] Other patient-reported outcomes such as patient satisfaction or patient knowledge were not collected in this study, and should also be considered. To our knowledge, a core outcome set has not yet been established around SDM and may be helpful for future research.

6.4.5 Administrative health data

Administrative health data is often limited by data accuracy issues. In future research, we recommend chart review studies to validate case definitions for OUD, anxiety and depressive disorders. Validation of the data during replication studies will substantially enhance internal validity in future research.

6.4.6 Epistemological limitations

Our pilot study (chapter 4) may inform future research regarding overcoming challenges for how to recruit, measure and study SDM. Chapter 3, approaches the study of SDM from a different lens of not investigating determination of the effectiveness of SDM, but inquiring around patient lived experience and better understanding whether person-centred approaches like SDM may be valued or desired by our target population. An effective intervention may be irrelevant if patients do not wish or refuse to use it. Although this approach contrasts epistemologically with our other quantitative methods, the knowledge obtained provides important context to the discussion around SDM in emerging adults. Finally, chapter 5 complements the dissertation by examining the potential longitudinal impacts of the primary mental health conditions under investigation in this dissertation – anxiety and depressive disorders. These are common conditions and by understanding their potential deleterious impact, this highlights importance and urgency to the overall field and body of work.

6.4.7 SDM in adults with anxiety disorders

No studies exploring the use of SDM in adults (18-64 years) with anxiety disorders were identified in our systematic review (chapter 2).However, SDM may be associated with a reduction in anxiety

symptoms among people with depression. In chapter 4, we found preliminary qualitative evidence suggesting emerging adults with anxiety and depression may value more involvement in their care planning. Future research around SDM is strongly recommended for people with anxiety disorders.

In summary, we recommend: i) a consensus on the definition of emerging adulthood; ii) a consistent operational definition and measurement of SDM; iii) the development of a standardized core outcome set for use in quantitative studies of SDM; iv) development of recruitment strategies tailored for emerging adults with mental health concerns; v) larger, longitudinal studies to investigate the impact of SDM on patient-reported outcomes; vi) more qualitative research to explore the individual lived experience of emerging adults with anxiety and depression who may not use conventional mental health services.

6.5 Implications for policy and practice

Over the past two decades, person-centred approaches to care have been associated with patient-reported outcomes such as improved HRQL, increased patient satisfaction, and decreased health utilization, which has been associated with a reduction in health system costs.[8,40] Person-centred care[40] is thought be an essential practice for advancing the following four key population health goals, known as the "quadruple aim"[41]: i) improving the patient and healthcare provider experience, ii) improving the health of populations, iii) reducing the per capita costs of healthcare, and iv) improving the work life of providers.[41] This framework encourages person-centred and integrated systems of care, often involving collaborative or team-based care. SDM has been considered to be the foundation of person-centred approaches to healthcare. Global health policy organizations such as the World Health Organization (WHO) have begun to recommend implementation of integrated and person-centred care within public health systems wordwide.[40,42] Despite widespread advocacy for person-centred care and SDM globally[43-45], little research has been conducted specifically in emerging adults suffering from mental health conditions.

This dissertation was successful in identifying several implications for public health policy and clinical practice. First, we found qualitative evidence that emerging adults may desire more knowledge about their mental health conditions and involvement in mental health-related decisions. Although, we found no peer-reviewed studies of emerging adults, the use of SDM appears promising and feasible among adults with depression[9-14], and may promote satisfaction

with care. SDM may be particularly suitable for individuals deciding various treatment approaches/plans for anxiety and/or depression. For example, there are approximately 30 different antidepressants (e.g., SSRIs) and several behavioural therapies (e.g., CBT) that often show similar effectiveness for both conditions in various patient populations.[46-48] However, unique individuals may respond differently to various antidepressants. Using an SDM or a person-centred approach may be beneficial for navigating the selection of treatment options for anxiety and depression.

There is presently insufficient evidence to suggest that SDM is necessary or desired in every clinical encounter in mental healthcare, suggesting a "one-size-fits-all" approach may be ineffective. Further, evidence from the peer-reviewed literature suggests that patients with more active mental health symptoms may be less likely to prefer SDM.[49,50] Moran-Sanchez *et al.*[49] found that individuals with a lower Brief Psychiatric Rating Scale rating was a significant predictor for preference for using SDM among patients with serious mental illnesses such as bipolar disorder or schizophrenia.[49] Authors of a systematic review in 2014 found twelve studies demonstrating that patients with major depressive disorder and schizophrenia commonly require extensive decision-making support.[3] These individuals commonly required more information around "basic facts", "treatment" and "coping" than patients with less severe mental illnesses.[50]

We recommend that it may be beneficial to assess whether a patient is able/willing to participate in SDM at each clinic visit to determine how to proceed. Due to our findings and review of the literature, we suggest the following scenarios may illustrate when SDM is not appropriate:

- If the patients is overwhelmed by their illness, and cannot cope/participate in decision-making.
- When their illness impairs the patient's capacity to act in their own self-interest.
- If the patient prefers to defer decision-making to a trusted caregiver/proxy or healthcare providers.

However, even for patients who experience any of the above, these circumstances are often not permanent. Patients have the right to exert their autonomy and to participate in their own health-related decision-making when capable and interested to do so.

This research identified several deleterious impacts of anxiety and/or depressive disorders in adolescents and emerging adults. For example, clinically significant symptoms of anxiety and/or depression, and low HRQL were associated with lower PHE scores during a clinic visit. Interventions that may reduce anxiety/stress prior to clinic visits may facilitate engagement. Future research would be required to explore this hypothesis further. In chapter 5, we learned that anxiety and/or depressive disorders were independent risk factors for OUD, and co-occurring alcohol-related disorders considerably exacerbate the risk of OUD. Therefore, our data suggest it is important for clinicians to consider substance use (including but not limited to, alcohol and opioids) in youth/emerging adults with anxiety and/or depression.

In conclusion, anxiety and/or depressive disorders pose considerable hazards to emerging adults including risk of OUD. Emerging adults commonly are reluctant to seek professional care, however social support and more person-centred approaches to care may facilitate treatment seeking and adherence. SDM is a promising approach for enhancing the quality of decision making and patient-reported outcomes among people with anxiety and/or depression; more compelling evidence is needed to better inform policy and practice, especially in light of the current knowledge gaps for emerging adults in the emerging field of public psychiatry.[51,52]

Public psychiatry aims to "provide advanced training to psychiatrists who are interested in engaging in clinical care, teaching and program/policy development and evaluation within the public sector", while facilitating "recovery-oriented systems of care to the most vulnerable individuals in society."[52] Future research around person-centred care and SDM may be needed to advance this field. In the interim, we recommend that SDM be discussed and offered to patients, ensuring the needs/values of different patients are met.

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APPENDIX

CHAPTER 7: Treatment options and shared decision-making in the treatment of opioid use disorder: A scoping review

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7.1 ABSTRACT

Background: Shared decision-making (SDM) is an approach to clinical decision-making inclusive of patients' values and preferences during health-related decisions. Previous research suggests SDM may be beneficial in the treatment of substance use disorders; however, the impact of SDM in the treatment of opioid use disorder (OUD) remains unclear.

Objectives: To identify relevant peer-reviewed literature related to SDM in adults (≥18 years) with OUD, and to summarize the findings according to relevant patient health and treatment-related outcomes.

Methods: A scoping review was conducted. Five electronic health databases were searched from database inception until September 2019. Only peer-reviewed studies where adults with OUD were provided a choice and/or allowed input into their treatment plan were included. Two independent reviewers screened, extracted, and assessed the quality of included studies.

Results: Fourteen studies (n=1,748 participants), including seven randomized controlled trials, three non-randomized controlled trials, two observational studies, and one qualitative study met inclusion criteria. Two studies showed a decrease in illicit drug use. One study showed improvements in treatment retention, satisfaction with care, quality of life, perceived dose adequacy and risk of arrest. One qualitative study suggested that inclusion of patients in treatment decisions may improve patient satisfaction, while excluding patients may encourage discontinuation of treatment.

Conclusions: The available evidence suggests that when clinicians provide treatment options and/or include patients with OUD in treatment-related decisions, outcomes may improve. However, more research is warranted to determine the impact of SDM in the treatment of OUD as few studies measured or evaluated SDM explicitly.

7.2 INTRODUCTION

Opioid use disorder (OUD) is a chronic remitting and relapsing disorder characterized by the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) as “a problematic pattern of opioid use that persists despite adverse consequences to daily life and/or functioning" over a period of 12 months.[1] An estimated 26.8 million people live with OUD globally [2], and it is associated with a high risk of preventable death.[3] In North America, deaths from opioid-related overdoses have increased nearly four-fold from 2010-2015.[4-6] From 2015 to present, the incidence rate of opioid-related deaths continued to climb past epidemic levels (i.e., beyond 15.0 per 100,000 people) – due to several suspected reasons such as increased: i) OUD prevalence, ii) illicitly manufactured and potent opioids such as fentanyl and carfentanil [5,7-10], and iii) barriers attributed to the COVID-19 pandemic.[11,12] The economic burden associated with OUD is immense. A systematic review in 2009 found that the economic burden of prescription opioid misuse alone cost in excess of $50B per year in the United States.[13,14]

The World Health Organization (WHO) has recommended the adoption of person-centred approaches to care to mitigate the global burden of chronic diseases.[15] WHO describes person-centred care as “an approach to address individual health across the full continuum of biological, psychological, social, and spiritual needs”.[15] Shared decision-making (SDM) has been considered by scholars as an essential tool for achieving person-centred care.[16,17] SDM is characterized by Elwyn *et al*., (2012) as an approach where "clinicians and patients share the best available evidence when faced with the task of making treatment decisions, and where patients are supported to consider options to achieve informed preferences."[18,19] SDM often includes patient involvement in various health decision-making processes, such as goal setting and treatment decision making.[19] Previous research suggests that SDM is beneficial for improving patient-reported outcomes such as satisfaction with care and treatment retention for patients with chronic diseases.[20-22]

Evidence from recent reviews suggests SDM may be feasible and beneficial for people in treatment for substance use and psychiatric disorders.[23-25] In 2016, a systematic review of studies of adult patients with a variety of substance use disorders was conducted by Friedrichs *et al.*[24] and the authors found SDM was associated with improved outcomes such as increased patient satisfaction, and increased treatment adherence with few reported adverse events. However, only a few studies

were included involving people with OUD. In 2019, a scoping review was conducted by Marchand *et al*.[25] and the authors found 149 references on patient-centred care in substance use disorder treatment, and 36% of those involved SDM, identified as "client and provider negotiation strategies." A systematic review by Fisher *et al.*[23] in 2020 found preliminary evidence that SDM may be feasible and beneficial in patients with concurrent substance or alcohol use and mental health disorders. However, it was unclear if SDM impacted patient-reported outcomes. Ethical concerns remain around the involvement of individuals with severe psychiatric or substance use disorders in treatment decisions, as there is evidence that cognition and decision-making may be impaired in some individuals.[26,27]

To our knowledge, the impact of SDM in the specific context of OUD treatment has not been systematically reviewed. We believe a scoping review may help address the important gaps in the literature regarding treatment of OUD. Moreover, the COVID-19 pandemic has further accelerated the drug overdose crisis[11], and more effective methods of managing the impact of OUD have been urgently requested by experts in the field.[28-30] Given the pressing nature of OUD, a scoping review on SDM within the specific context of treatment for OUD may help identify key gaps in the evidence and help guide urgently needed clinical research.[31]

7.2.1 Objectives

The objectives of this scoping review were to: i) establish the breadth and depth of the relevant scientific literature related to SDM in the treatment of OUD in adults (≥18 years), and ii) summarize the main findings according to relevant patient health and treatment-related outcomes.

7.3. MATERIALS AND METHODS

In this scoping review, we followed the methodological framework outlined by Arskey & O'Malley[32], Daudt *et al.*[33] and Levac *et al.*[34] We then used the PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation[35] to guide the reporting of this review. Stakeholders were consulted at each stage of the review process to ensure the relevance of this work. Detailed methods for this scoping review were previously published elsewhere.[31]

7.3.1 Information sources

We consulted a health research librarian with expertise in developing search strategies for systematic and scoping reviews and then searched five electronic health databases: MEDLINE, EMBASE, PsycINFO, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews. The electronic databases were searched from inception until September 2019. We also searched reference lists of included studies and related systematic reviews.[24,25] OUD experts were contacted to suggest any additional studies. Duplicates were removed, and the retrieved studies were assessed for inclusion. For feasibility reasons, the search was limited to articles published in English-language.

7.3.2 Search strategy

Our multidisciplinary team developed a comprehensive preliminary search strategy in consultation with expert stakeholders and a health research librarian. We consulted other relevant systematic reviews [22,24] in this field and developed a search strategy using free text search terms and Medical Subject Headings (MeSH) related to OUD and SDM. We thought of SDM as a broad construct that includes concepts such as "patient participation," "patient preferences," "patient engagement," "patient autonomy," "decision-making," "self-care," "decision support," "consumer engagement," and "consumer participation." As a result, we included all of these terms in our search strategy. During protocol development, the search strategy was pilot tested by screening 100 articles for inclusion. The lead author then consulted with a health research librarian to revise the search strategy to maximize effectiveness and efficiency. The preliminary MEDLINE search strategy can be found here (**S1**).

7.3.3 Study selection process

After pilot testing the search strategy, two reviewers then independently screened titles and abstracts, then reviewed the full text of studies that met the inclusion criteria. Additional authors were consulted to arbitrate any disagreements during screening. **FIGURE 1** displays the included and excluded studies using a PRISMA-flow diagram.[36]

7.3.4 Eligibility criteria

The Population Intervention Comparator Outcome Study design/type (PICOS) model [37] was used as a guide for developing an eligibility criteria framework. Please see **TABLE 1** for a complete list of the inclusion and exclusion criteria.

Population: Studies were included if they focused on "opioid dependence" or "opioid addiction," as classified in the DSM-IV or prior versions in adults (18 years or older) diagnosed or undergoing primary treatment for OUD per the Diagnostic and Statistical Manual (DSM) or International Classification of Diseases (ICD) criteria. Adults enrolled in methadone maintenance programs for substance use disorder, and studies of "heroin users" were assumed to have OUD. Studies were excluded if participants included individuals mandated to treatment by law (e.g., through a civil commitment or a diversion program).

Intervention: We included studies that either: i) explicitly studied SDM according to Elwyn *et al.*[18,19] definition; or ii) studies that reported patients were given a choice or allowed input into decisions regarding their treatment plan. SDM was defined by Elwyn *et al*.[19] as i) deliberation of various health options; ii) informed patient choice and decision support, weighing the benefits and risks of each approach; and iii) a collaborative decision with a health care provider.

Comparison: A control condition was not required for inclusion.

Outcomes: We included all patient outcomes associated with OUD treatment. Studies that only reported healthcare provider outcomes were excluded.

Study type: The following study types were included for review: experimental studies [e.g., randomized controlled trials (RCTs)], quasi-experimental studies (e.g., controlled designs without randomization), observational studies (e.g., cross-sectional surveys, case-control, and prospective and retrospective cohort), and qualitative studies. Case-reports and editorials were excluded. The included studies from potentially relevant systematic reviews were cross-referenced with our search to ensure comprehensiveness.

7.3.5 Data extraction

In consultation with the senior author, two reviewers pilot-tested the data extraction forms to ensure all relevant data items were identified. Once the extraction form was finalized, the two

reviewers then independently extracted the relevant data. An additional author was consulted to arbitrate any disagreements and reach a consensus, if necessary. We extracted the following information: 1) bibliographic characteristics (e.g., author, year), 2) methodological characteristics (e.g., intervention type, outcomes), 3) main findings, and 4) SDM-related findings (e.g., identification of whether patients were provided treatment options during the study). Copies of these data may be accessed from the corresponding author.

7.3.6 Critical appraisal of the included studies

We used the Mixed Methods Appraisal tool (MMAT)[38] to assess the quality of the included studies. Two reviewers independently assessed each study and settled any discrepancies by discussion.

7.3.7 Synthesis of results

Aligning with the objectives of our review, we conducted a narrative synthesis summarizing the results of the included studies according to patient health outcomes. The quantitative and qualitative literature and outcomes related to SDM were charted and reported separately.

7.4 RESULTS

7.4.1 Selection of sources of evidence

FIGURE 1 shows the study selection process and reasons for exclusion via PRISMA-flow diagram. We identified n=1,154 articles via electronic database search and after independent screening and searching of reference lists. Fourteen studies (n=13 quantitative, n=1 qualitative) met the final inclusion criteria, comprising of n=1,748 participants. Publication dates spanned from 1981 to 2018.

7.4.2 Characteristics of included studies

TABLE 2 charts the characteristics of the included studies. Among the included studies, nine were conducted in the United States, two were conducted in the United Kingdom, two were conducted in Spain, and one study was conducted in Canada. According to MMAT[38] study definitions, seven quantitative randomized studies (i.e., RCTs)[39-45], three quantitative non-randomized controlled

trials[46-48], and three quantitative descriptive (i.e., observational studies)[49-51] and one qualitative study[52] were analyzed. Eleven studies[40-48,50-52] included participants enrolled in methadone maintenance treatment, and two studies[39,49] administered buprenorphine as the pharmacological treatment. Four of the interventions compared either self-regulated or negotiable methadone dosing to mandatory practices (treatment as usual).[40,43,44,48] Four studies offered optional counseling or psychotherapy[41,45-47], two studies gave participants a choice between office-based or home-based buprenorphine inductions.[39,49] One study provided choice of inpatient or outpatient opioid detoxification.[42] SDM was neither explicitly evaluated nor measured with an instrument in any of the included studies. Only one study[46] reported that patient input into treatment decisions was supported or encouraged, as suggested by Elwyn *et al.*[18] criteria for SDM.

7.4.3 Main findings

TABLE 3 charts the main findings and authors' conclusions.

7.4.3.1 Quantitative synthesis

Thirteen quantitative studies were identified comprising 1,729 individuals. Nine studies[39,41,43-48] reported whether providing patients with treatment options (e.g., self-dose regulation) impacted patients' illicit drug use, comprising 1,392 individuals. Two studies[43,48] observed decreased illicit drug use as a result of providing patients with OUD treatment options. Seven studies [40,41,44-47,49] reported treatment retention, totaling 1,325 individuals. Among these studies, one RCT of 300 participants[44] observed a statistically significant increase in treatment retention, while the remaining studies observed no statistically significant difference. Health-related quality of life was reported in one study [45] consisting of 300 participants, and a statistically significantly improvement was observed.[45] One study of 54 participants found that involving patients in treatment decisions may reduce arrest rates.[47]

An RCT of 300 participants[41] found no difference in cost between patient-centred methadone and treatment as usual. Another study[46] reported that patient-centred methadone did not impact the frequency of therapist or healthcare provider visits. One RCT of 60 participants[42] found that when participants were matched with their preferred detoxification method (either inpatient or outpatient) no significant impact on abstinence rates had occurred. However, the authors noted the

group that received their preferred method tended to "do better," but no other outcomes were measured. One observational study of 123 individuals[50] found that when patients were matched with their treatment preference, satisfaction with care improved. A secondary analysis [51] involving 122 individuals from the aforementioned study[50] found that when patients were matched to their treatment preferences, perceived adequacy in methadone dose improved. Only one quantitative study[49] reported adverse events and reported one instance of hospitalization for one participant who was enrolled in a home-based induction group.

7.4.3.2 Qualitative synthesis

One qualitative study involving 19 participants[52] was included in the review. Sanders *et al.*[52] interviewed 19 adult patients in methadone maintenance therapy and sought to gain feedback about their methadone dosing preferences that were provided during treatment. Patients expressed a desire for a "shared decision-making model," where comfort in treatment decisions was influenced by their perceived role in treatment decision making. Some participants felt they were not always in control of their treatment decisions, which commonly facilitated a desire to discontinue treatment. This feeling of lacking control was expressed via metaphors of incarceration (e.g., methadone as "liquid handcuffs"). In addition, in this study participants expressed how they desired to avoid any negative effects associated with methadone treatments. The adverse effects mentioned included feeling "numb," weight gain, insomnia, and constipation.[52]

7.5 DISCUSSION

To our knowledge, we have conducted the first scoping review of SDM in the context of OUD care. SDM has shown promise and is being evaluated for implementation in other areas of medicine, such as primary care and in the treatment of substance/alcohol use and psychiatric disorders.[53-56] However, SDM has not yet been systematically reviewed in the specific context of OUD.[57] Among the included quantitative studies we found preliminary evidence that either i) providing adults with OUD treatment options or ii) the use of SDM as defined by Elywn *et al*. 2010[19] may be feasible and potentially beneficial. Findings from the qualitative studies indicate that people with OUD may prefer and potentially benefit from being provided treatment options or participating in SDM. However, we suggest interpreting the results with caution for several reasons. First, the impact of SDM on health-related outcomes was mixed with some studies

showing positive results, while others showed no improvement. Secondly, heterogeneity among the studies precluded meta-analysis to determine estimates of treatment effect. While little evidence of harm was identified in the included studies, the reporting around harms was not clear. For instance, one study reported that they did not incorporate adverse events reporting into their outcomes.[39]

7.5.1 Limitations within included studies

Several additional limitations among the included studies prohibited us from generating conclusions about the impact of SDM on patient outcomes. Despite performing an inclusive search of five health databases for articles broadly related to SDM, we found only one article that explicitly used the language "shared decision-making," and only two articles reported providing i) treatment options and ii) decision-making support, consistent with the definition of SDM set forth by Elwyn *et al.* 2010.[18,19] For example, in a majority of the included studies, treatment options for OUD patients were restricted to only choices around OAT dose, or treatment setting (e.g., home or clinical induction), while a few permitted optional adjunctive psychotherapy. From the included studies, it was unclear how much input patients were permitted to have in decisions around setting health goals or selecting evidence-based medications approved for OUD. This may suggest that SDM is not commonly practiced, or practiced in a limited capacity, in settings that treat OUD. Moreover, the included studies lacked sufficient descriptions if and/or how providers educated or supported patients to make "informed decisions" as described by Elwyn and colleagues.[18,19] None of the studies measured the occurrence of SDM with a validated instrument, which produces uncertainty as to what extent SDM occurred, and whether the quality of SDM was sufficient to yield any observable benefits.

7.5.2 What this scoping review adds

This scoping review highlights substantial gaps in the evidence around the use of SDM in patients with OUD. For example, we excluded two articles involving patients with OUD that were included in the Friedrichs *et al.*[24] systematic review. These articles focused solely on general patient preferences of OUD treatment, rather than the impact of providing treatment options or SDM on health outcomes. Our findings are consistent with other reviews that have examined the impact of SDM in the treatment of other substance and alcohol use disorders.[24,25] This is consistent with the

findings of a more recent systematic review by Fisher *et al.* 2020[23], which found preliminary evidence that SDM supports "acceptability, feasibility and utility in managing mental health and alcohol use disorder comorbidities," but their review did not specifically investigate the impact of SDM in OUD treatment on health outcomes. Our scoping review expands upon these reviews by identifying several critical knowledge gaps in this field pertaining to the use of SDM in treatment for OUD, which often varies substantially from other substance use disorders. Our findings may be viewed in context with a recent systematic review of six studies that found no evidence in support of compulsory treatment options for adults with substance use disorders, and the potential for harms were noted.[58] Additionally, a recent qualitative study of 283 people, that did not fully meet criteria for our review, found that among individuals in methadone treatment, patients may not be aware of treatment alternatives.[59] The authors concluded that the availability of additional medication options (e.g., buprenorphine) "highlights a need for clear communication between clinicians and patients."[59] These findings were consistent with the findings from Sanders *et al*.[52] who also reported that patients may feel a "lack of participation/control in treatment" and may "value a shared decision-making model."

7.5.3 Strengths and limitations of the review

The methods protocol for this work was peer-reviewed and published *a priori*.[31] This scoping review performed a robust search strategy using a broad range of search terms acquired from previous systematic reviews and reference lists were searched. Two independent reviewers screened, extracted and analyzed the data. Feedback from stakeholders and international OUD experts was collected throughout the review. Our scoping review also assessed the quality of the included studies, which may be useful for future research and policy. For feasibility reasons, we only included studies written in the English language, which may have limited the scope of our review by excluding potentially relevant works published in other languages.

7.5.4 Conclusion

Peer-reviewed research on SDM within the specific context of the treatment of OUD is lacking in breadth, depth and quality. Our results, when taken into context with the previous literature, suggest SDM may be feasible in adults with OUD. Future high-quality controlled studies are warranted to determine whether the use of SDM is beneficial for adults with OUD.

7.5.5 Recommendations for future research

In future studies, we recommend the development of a consistent and accepted operational definition of SDM, including its measurement with a validated instrument such as the OPTION-tool[60] or the ASK-MI tool.[61] Additionally, we suggest the development of a clinically relevant outcome set for OUD that is developed in collaboration with patients or people with lived experience.

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7.7 ADDITIONAL INFORMATION

7.7.2 Competing interests

We have no competing interests to declare.

7.7.3 Funding statement

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7.7.4 Patient consent

Not required.

7.7.5 Acknowledgements

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7.8 TABLES

7.8.1 TABLE 1. Inclusion/exclusion criteria

	Included	**Excluded**
Population	• Diagnosis of OUD (DSM-V) • Opioid or heroin dependence (DSM-IV or prior versions), or; • Patients enrolled in methadone maintenance or opioid dependency programs, or; • "Heroin users" • Other mental or physical health comorbidities in addition to OUD, and; • Mean age ≥ 18 years	• Studies inclusive of participants <18 years in which adults ≥ 18 could not be analyzed separately • Substance use disorder without evidence of OUD (e.g., methadone prescription) • Opioid dependence in chronic cancer pain (e.g., hospitalized patients)
Intervention	• Shared decision-making as defined by Elwyn *et al*. criteria, or; • Involved patients that were given a choice or allowed input into their treatment plan.	• Studies that did not provide patients with any options or choices regarding their treatment plans/decisions (e.g., treatment was mandated)
Control	• Studies with or without control groups.	• None.

Outcomes	Any outcome related to OUD treatment, including: • Illicit substance use • Mental health symptoms • Sociobehavioral • Physical health	• Healthcare provider outcomes that could not be analyzed separately. • Studies without outcomes
Study type	• Quantitative studies (e.g., controlled studies, observational studies) • Qualitative studies • Systematic reviews and meta-analyses	• Non-peer reviewed literature (e.g., abstracts or conference proceedings) • Articles not in English-language • Animal studies • Case studies

7.8.2 TABLE 2. Characteristics of included studies

Author, Year, (Country)	**Study characteristics**	**Participant characteristics**				**Methodological characteristics**		
	Study type (MMAT)	**Inclusion criteria**	**Sample size**	**Mean age (SD)**	**N (%) Male**	**Intervention**	**Control**	**Outcomes**
Brands *et al.*, 2003 (USA)*****	Quantitative non-randomized	OUD diagnosis; in methadone treatment	217	35	109 (50.4)	Patient-centred methadone maintenance program	MMT with treatment contingent on abstinence and mandatory counselling	Treatment retention; illicit drug use; mean number of physician/therapist visits
Cunningham *et al.*, 2011 (USA)*	Quantitative randomized	Opioid dependent	79	43	58 (73.4)	Group 1: standard of care office-based	NA	Self-report of opioid use; self-report of any drug use

		(DSM-IV); in buprenorphine induction; HIV+				induction; Group 2: patient-centered home-based induction		
Dawe *et al*., 1991 (UK)**	Quantitative randomized	Opiate dependent; daily users	39	26 (4)	26 (70.3)	Patient negotiated methadone dose levels and the rate of reduction	Fixed detoxification schedule	Treatment completion; treatment retention; dose levels; treatment compliance
Desmond & Maddux, 1983 (USA)****	Quantitative non-randomized	Opioid users enrolled in methadone maintenance treatment	54	33.4	48 (88.9)	Optional psychotherapy	Mandatory psychotherapy	Treatment retention, employment, illicit drug use, arrests

Dunlap *et al.,* 2018 (USA)**	Quantitative randomized	Met DSM-IV opioid dependence criteria	300	43.0	NR	Patient-centered methadone treatment	Usual methadone maintenance treatment	Treatment retention, unit and weekly costs of services, drug use, patients meeting the DSM-IV criteria for opioid dependence
Gossop *et al.,* 1996 (UK)*	Quantitative randomized	Physically dependent on opiates and were asking to be withdrawn	60	26.1 (5.12)	45 (75.0)	Choice of inpatient or outpatient withdrawal program	NA	Rate of complete withdrawal from opioids (abstinence), patient choice of treatment, maintaining contact with clinic

Havassey & Hargreaves, 1981 (USA)**	Quantitative randomized	Heroin addicts in methadone maintenance treatment	85	35	60 (70.6)	Self-regulated methadone done with/without additional take-home dose privileges	Standard methadone maintenance treatment	Methadone dosage, illicit drug use, attrition
Maddux *et al.,* 1995 (USA)*	Quantitative randomized	Eligible for methadone maintenance treatment	300	36.3	229 (76.3)	Self-regulated methadone dose	Standard methadone treatment	Retention, Methadone dosage, Outcomes after 1 year retention
Robles *et al.,* 2001 (USA)**	Quantitative non-randomized	Enrolled in methadone maintenance treatment	57	43.6 (5.01)	36 (63.2)	Self-regulated methadone dose	Standard abstinence-based take-home dosing procedures	Opioid positive urine specimens, evidence of methadone diversion, methadone dose

Sanders *et al.,* 2013 (USA)***	Qualitative	Enrolled in methadone maintenance treatment	19	NR	10 (52.6)		NA	Patient perceptions about methadone dosing, meanings associated with methadone treatment, patient adherence
Schwartz *et al.*, 2016 (USA)***	Quantitative randomized	Newly admitted methadone patients, aged 18 and over	295	42.7(SD=10.1)	177 (59.0)	Patient-centered methadone maintenance treatment consisting of optional counseling	Treatment as usual methadone maintenance treatment	Opioid-positive urine tests, percentage of cocaine-positive urine screens, self-reported number of days of heroin and cocaine use in the 30 days prior to the interview were obtained from the Addiction Severity Index, DSM-IV opioid and cocaine

								dependence diagnoses, HIV drug and sex risk , Quality of Life Global Scores, treatment retention in the original opioid treatment program
Sohler *et al.,* 2010 (USA)*****	Quantitative non-randomized	(a) at least 18 years old, (b) Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) opioid-dependent, and (c)	115	44.9 (SD=8.5)	85 (73.9)	Patient choice of buprenorphine induction at home or the physician's office.	N/A	Induction difficulty, treatment retention, 30-day drug use

		insured by a health plan accepted at the health center or ability to pay for treatment on a sliding scale fee.						
Trujols *et al*., 2012 (SPA)****	Quantitative non-randomized	Methadone-maintained, heroin-dependent patients (DSM-IV) who had received MMT at their respective centres for at	123	38.8 (SD=7.5)	91 (74.8)	Survey using the Verona Service Satisfaction Scale for Methadone Treatment (VSSS-MT), and the General	N/A	Acceptance of the survey, perceived participation in methadone maintenance treatment, satisfaction with methadone as a medication, desired adjustment of methadone dose,

		least 3 months.				Health Questionnaire-28 (GHQ-28).		psychological adjustment
Trujols *et al.*, 2017 (SPA)***	Quantitative descriptive	Methadone-maintained, heroin-dependent patients who had received MMT at their respective centres for at least the previous 3 months.	122	38.8 (SD=7.6)	92 (75.6)	Administration of the Visual Analogue Scale of Methadone Dose (VAS-MD)	N/A	Satisfaction with MMT, opinion of methadone as a medication, psychological distress, perception of methadone dose adequacy, perceived participation in methadone dosage decisions

Footnotes: * = Number of MMAT criteria met

7.8.3 TABLE 3. Summary of results

Author, year	Main findings	Author's conclusions
Brands et al., 2003	Across the three cohorts: there was a significant reduction in the number of patients with any opioid use ($F=18.6$, $p<0.0001$) over the first six months in treatment; the percent of patients with any opioid use fell from 98.2%, 87%, 86.5% in month 1 to 60.6%, 70.1%, 50% in month 6; the number of physician visits increased linearly (13.6 ± 0.8, 17.7 ± 0.9 and 22.5 ± 0.8, respectively; $p=0.0001$); first cohort: patients saw a physician a mean of 6 times in month 1, decreasing to once a month by month 4; second cohort: total number of visits with program therapists was slightly lower, but returned to initial levels in the third cohort (25.4 ± 1.3, 20.6 ± 1.6, and 23.8 ± 2.1, respectively; $p=0.006$); third cohort: on average patients saw a physician 8 times in month 1; this leveled off to about 3 times by month 3; on average patients in the first and last groups visited a therapist seven times in the first month of treatment, decreasing to four times per month in the next three months and three times per month by month 6; two-year cumulative MMT retention in the three cohorts was 73%, 69%, and 67% respectively.	Despite the shift to a patient-centred approach, patients were still able to decrease and maintain a reduction in opioid use. When counselling became elective the patients continued to visit therapists as often as when the service was mandatory. The increased and individualized methadone doses along with the availability of increased on-site services in response to patients' needs were likely factors that enabled the high retention rates to be maintained. In conclusion, after the program changes were implemented, there was no deleterious impact on treatment outcomes.
Cunningham et al., 2011	Among all participants, opioid use declined from 88.6% at baseline to 42.0% at 1 month, 33.3% at 3 months, and 27.3% at 6 months; significant reductions in opioid use occurred between baseline and 1 month (OR=0.09, 95% CI=0.04–0.22), between baseline and 3 months (OR=0.06, 95% CI=0.03–0.15), and between baseline and 6 months (OR=0.05, 95% CI=0.02–0.12); no significant reduction found between 1 and 3 months or 3 and 6 months; any drug use also declined from 91.1% at baseline to 56.5% at 1 month, 43.1% at 3 months, and	Our study, which compared two different buprenorphine induction strategies, found that patient-centered home-based inductions were feasible and preferred by most of the participants. As innovative treatment strategies related to buprenorphine inductions are emerging, it is essential that they

	36.4% at 6 months; significant reductions in any drug use occurred between baseline and 1 month (OR=0.13, 95% CI=0.05–0.31), between baseline and 3 months (OR=0.07, 95% CI=0.03–0.18), and between baseline and 6 months (OR=0.06, 95% CI=0.02–0.14); there was no significant reduction between 1 and 3 months or between 3 and 6 months.	be based on established theories or models and be well studied to optimize treatment outcomes for opioid addiction.
Dawe et al., 1991	17% (n=3) of the negotiable group completed treatment compared to 53% (n=8) of the fixed group ($p<0.05$); 29% (n=7) of the negotiable group were non-completers at 70 days and still using a mean dose of 21 mg methadone (SD=15), range 5-50 mg; the mean dose reduction during detoxification was significantly greater in the fixed group, with a mean reduction of 38 mg (SD=13.4) compared to 25 mg (SD=19) in the negotiable group ($r=2.27$, $p<0.05$); there is no statistically significant difference between the two groups in retention rate at 42 days, the last point at which both groups are directly comparable, with 8 (53%) of the fixed group still in treatment and 12 (50%) of the negotiable group still in treatment (Chi square=0.41, $p=0.84$).	Flexibility within a short-term outpatient withdrawal programme did not produce the improvement in completion rates nor a reduction in overall methadone dose found in an in-patient or structured day clinic setting. A comparison of the two groups during the first 6 weeks showed no improvement in retention rates for the negotiable group when compared to the fixed group. However, where retention in treatment is a priority, other types of interventions should perhaps be considered in preference to short-term detoxification programmes which are most suitable for individuals wishing to become abstinent.
Desmond & Maddux, 1983	Mean methadone dose and mean number of adjustments in dose were nearly identical between groups. Differences in the number of psychotherapy sessions and the number of hours spent with the patients were statistically significant. On average, Counselor M (mandatory) had twice as many contacts and spent more	Our study did not demonstrate that frequent, mandatory psychotherapy led to significantly better outcomes

	time with patients. On several criteria, patients in the optional group did somewhat better than those in the mandatory group; they remained in treatment longer, had a lower mean percentage of urines positive for morphine, and fewer felony arrests during treatment. However, the optional group had comparatively fewer mean months of employment. One of the differences reached statistical significance: percent of urines positive for morphine was significantly higher for the mandatory group.	than did pragmatic counseling with optional psychotherapy.
Dunlap et al., 2018	One-year retention rates were similar, with 49% of patients in the PCM condition and 46% in the TAU condition still enrolled in the original OTP at 12-month follow-up. Overall, PCM patients had slightly higher average treatment costs of $2395, compared to $2292 in TAU (not statistically significant); TAU and PCM patients had comparable negative opioid urine screening test results (40% of TAU patients at 12-month assessment compared to 39% of patients in PCM); TAU economically dominated PCM with a lower average cost and similar average outcome (small differences); on average, 40% of PCM patients did not meet the DSM-IV criteria for opioid dependence, compared to only 31% of TAU patients. This suggests that a greater percentage of PCM patients are less likely to be opioid dependent at 12 months following treatment entry.	The findings from this study suggest that patient choice concepts that allow them more control over certain treatment aspects can be introduced into standard methadone treatment without significant impacts or costs or patient outcomes. This should be a consideration for policy makers and providers as interventions to increase patients' treatment engagement are explored
Gossop et al., 1996	We also compared the other main treatment factor: whether the patient was randomly assigned to treatment or had chosen a particular option. This failed to show any significant effect at the 5% level, although subjects who expressed a clear preference tended to do better than those who expressed no preference and were assigned to inpatient or outpatient withdrawal at random	The effect of patient preference for either inpatient or outpatient withdrawal was not significant. The complete failure of the randomised outpatient group suggests, however, that inpatient options should be preferred (if available) unless the addict has

	(X=2-7, p=0 10). Twenty three of the 40 patients in the preferred group (58%) were successfully withdrawn, compared with only seven of the 20 patients in the random group (35%).	strong preferences for outpatient withdrawal. These results show that-opiate addicts can be withdrawn with a satisfactory level of success on an inpatient basis. It is not clear, however, what the wider implications are for outpatient withdrawal schemes.
Havassey & Hargreaves, 1981	The three randomly assigned treatment groups did not differ significantly in mean daily dosage of methadone prior to the experiment. The control group women showed a dramatic reduction in mean dosage level after week 12. While the other five groups all showed a slight downward dosage trend over time, other group differences are mostly accounted for by random variation in baseline dosage level. The control group showed increased illicit opiate use over its baseline value, while the two self-regulation groups showed no such increase; treatment assignment had a significant effect, reflecting the higher abuse rate in the control group. There were no effects of treatment assignment on detected use of either amphetamines or barbiturates, as examined by chi-square tests of association. None of the termination rates differed significantly across treatments.	The major result of the study suggests that the opportunity for increased take-home privileges was not an adequate incentive to induce methadone maintenance clients as a group to significantly decrease their ongoing maintenance dosage voluntarily. Treatment differences were seen in dosage trends (among the women) and in the use of illicit opiates. In both cases, however, these effects represented changes from baseline in the control group, while the two self-regulation groups showed little, if any, change. This is contrary to expectations. In ongoing maintenance treatment one would not expect changes of the sort observed in the control group. Yet the study did not change the treatment situation of the control subjects in any way that can plausibly account for our findings.

Maddux et al., 1995	15% of the patient-regulated dose group, 6% of the standard treatment group and 1% of the optional counseling group had maximum doses of 80 mg or more; the percentage of the optional counseling group retained in treatment exceeded that of the other two groups in 9 of the 12 months. At the end of the year, 60% of the optional counseling group, but only 50% of the patient-regulated dose group and 50% of the standard treatment group, remained in treatment; during the 30 days preceding the first anniversary of admission, the differences among the groups were small and non-significant; with respect to illicit use of drugs and other outcomes, the three subgroups did about equally well.	Allowing patients to regulate their methadone dosage did not lead to a general escalation of dose. This finding conforms to those of preceding studies cited. The mean of the maximum methadone doses of the subjects who regulated their own doses, 58 mg, exceeded that of subjects in standard treatment, 53 mg (not significant).
Robles et al., 2001	As shown in Fig. 2, the maximum dose dispensed during baseline was 165 mg. During the self-regulated dosing period, the maximum dose dispensed peaked at 300 mg and then decreased to 265 mg. A paired comparison of average methadone doses by patient revealed only a small but statistically significant increment from 76.84 mg during baseline to 80.04 mg during the self-selected dosage period ($W= 473$, $n = 57$, $p = 0.01$). Interestingly, although the number of doses in excess of 100 mg increased during the self-regulated dose period, 89.7% of the doses selected remained between 17 and 100 mg. A paired comparison of the percent of monthly opiate positive specimens (see Fig. 3) revealed a significant decrement from 5.26% during baseline to 1.64% during the self-selected dose period ($W= 169$, $n = 57$, $p < 0.01$). On the other hand, urinalysis results for amphetamines, benzodiazepines, cocaine, and THC remained unchanged with an average of 10% of the specimens being positive for illegal drugs. During the entire 22-month period, all patients required to return to the clinic to demonstrate possession of take-home doses were able to do so. In addition, local and state police, as well as the	For the sample of 57 patients who remained in MMT during the 22-month assessment interval, the maximum dose dispensed increased to a peak of 300 mg, while the average daily dose increased only 3.2 milligrams during the 16month self-regulation period. Although the number of doses greater than 100 mg increased during the self-regulated dosing period, almost 90% of all doses selected remained in the 10 to 100 mg window. These results concur with previous reports indicating that when given the opportunity to self-regulate their dose, methadone patients do not seem to abuse the system or ingest massive amounts of medication.

	DEA, reported that they had encountered no instances of liquid methadone diversion in the area during this study.	
Sanders et al., 2013	Participants valued a shared decision-making model. Their perceived role in making decisions about dose adjustment influenced their "comfort" in treatment. Perceived lack of control exerted a downward pressure on perceptions of ideal dose, often making participants feel they wanted to stop taking methadone altogether. Participants expressed lack of control through metaphors of incarceration: for example, treatment as "a life-long sentence;" and methadone as "liquid handcuffs." Urine drug screens were seen as a unilateral form of control in decisions about dose adjustment. "Dirty urines" (urine specimens revealing illicit opiate use) often resulted in automatic dose increases, which participants felt was unfair. One participant noted that it felt like treatment providers raised doses "without my consent" and did so "[because of] dirty urines; but [they] are not asking me why am I still getting high."	Perceptions about methadone dosing influence treatment effects at different doses. This is the "meaning effect" of the methadone. It may explain some of the tension, sometimes evident between providers and patients, between the medical understanding that the appropriate dose is the one that works (no matter how high) and the patient perception that certain doses feel too high and/or inappropriate. Participants in our study, who almost uniformly wished to discontinue methadone treatment at some point, felt that certain doses compromised their ability to successfully leave treatment in the future. For MMT patients, the dose represents something larger than its effect on reducing craving or preventing withdrawal; thus a model that only takes into account this narrow clinical dichotomy will be incomplete. The alternative model we propose illustrates the ways in which perceptions about methadone dose affect the experience of treatment. The model considers intrinsic and

		extrinsic factors exerting upward and downward pressure on perceived dose appropriateness and adds nuance to understanding of the acceptability (and perhaps effectiveness) of certain doses.
Schwartz et al., 2016	There was no significant difference between study condition for the percentage of participants with opioid-positive urine screens at 12-month follow-up; no significant differences by study condition were found for secondary outcome variables of cocaine-positive urine screens, self-reported heroin and cocaine use, meeting DSM-IV opioid and cocaine dependence criteria, HIV risk behaviors, aggregate physical and mental health quality of life or treatment retention at 12 months; for Quality of Life Global Score, PCM participants reported a significantly higher mean score than TAU participants (mean =3.70 and 3.47 for PCM and TAU respectively; difference=0.23, 95% CI=0.01–0.45; p = 0.04).	Findings suggest that requiring counseling is not demonstrably better than allowing patients to choose how much individual or group counseling they find valuable. Whether these findings can have an influence on the behavior of counseling staff, many of whom believe that patients will not change behavior without some coercion, or on accreditation bodies or regulatory agencies, is uncertain. Currently in the United States, funding of treatment is entwined intricately in a package of services that includes supervised methadone administration, drug testing and evidence of counseling attendance. Any changes in this package will require re-thinking the essential elements of MTPs and how these elements should be reimbursed.
Sohler et al., 2010	A similar proportion of people in each induction group experienced difficult inductions: 10 of 60 (16.7%) in office based inductions vs 8 of 47 (17.0%) in home-	We conclude that both office and home-based buprenorphine inductions are feasible in the

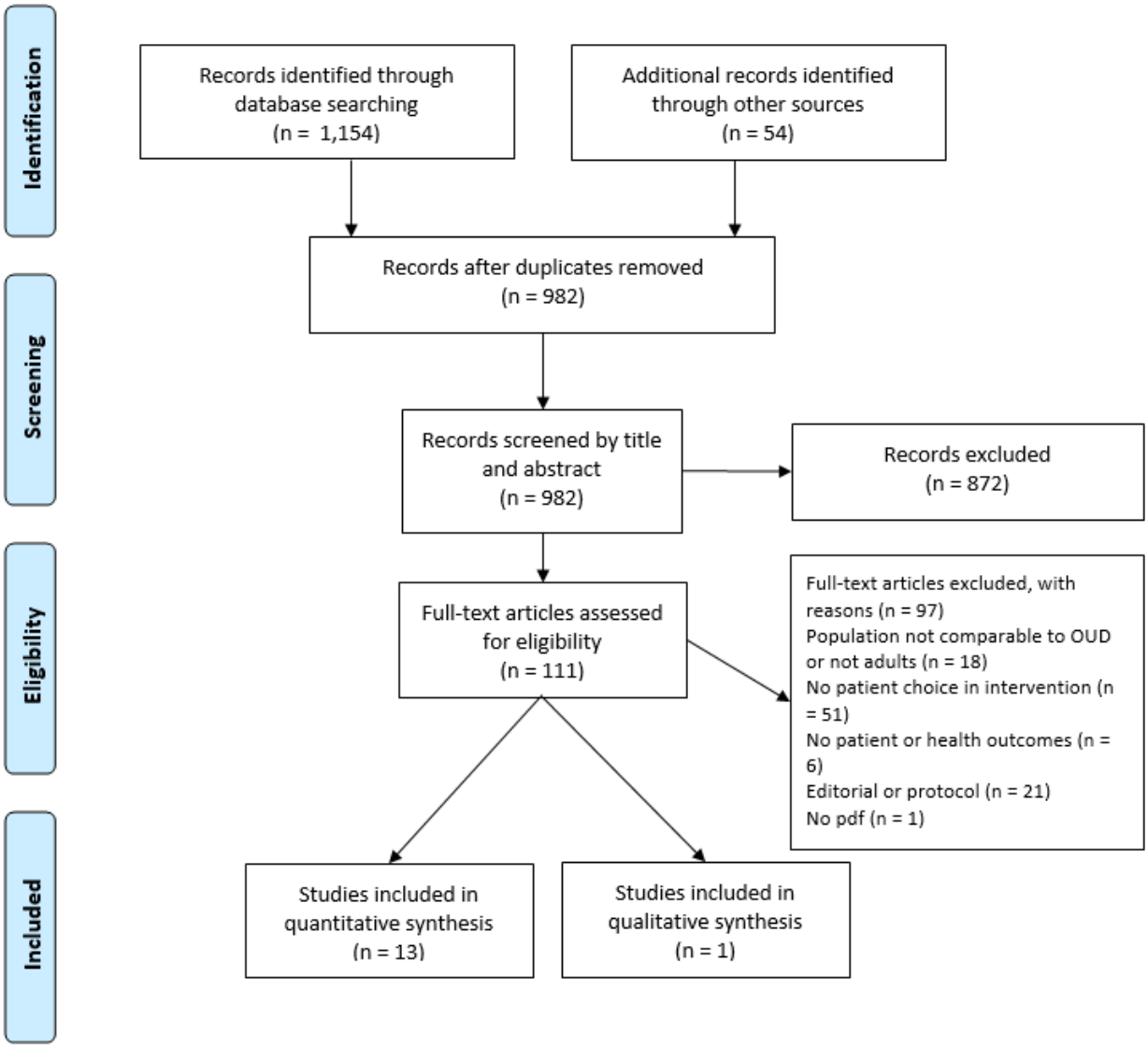
	based inductions (OR=0.98, CI=0.35-2.70); 30 day treatment retention was similar by induction type: 50 (78.1%) for office-based inductions vs 40 (78.4%) for home-based inductions (OR=0.98, 95% CI=0.40-2.40); insurance status and use of street methadone in the 30 days before induction were associated with 30-day treatment retention; these factors were also modestly associated with induction type in the full sample (30-day retention for office- vs. home-based induction, AOR=1.10, 95% CI=0.43-2.78).	primary care setting. In our study, treatment retention of 78.3% at 30 days is similar or greater than that reported in previous studies, and adds to the growing literature that demonstrates that patients can successfully undergo buprenorphine induction in office-or home-based settings. In contrast to our hypothesis that a strategy that encourages patient self-management from the earliest stage of treatment for opioid dependence would result in better retention, our data do not support either office- or home-based inductions as being superior with regard to short-term patient retention. Our evaluation of differences between patients who are retained at 30 days and who initially chose office- vs. home-based inductions indicate that, in most cases, patients and providers were able to appropriately assess patients' needs and self-management abilities and made appropriate induction strategy decisions.
Trujols et al. 2011	Of the 174 surveys originally intended, 20 could not be carried out; Those patients who refused to participate in the survey, compared with those who accepted, were younger (35.5 (SD=5.8) vs. 38.8 (SD=7.5) years,	As far as we are aware, this study represents the first attempt to assess both mental health status and satisfaction with

	t(145)=2.30, p=0.023) and had stayed shorter on their current MMT episode (26.8 (25.3) vs. 41.1 (43.5) months, t(83.52)=2.26, p=0.027); with regard to changes in methadone dose by physicians, 73.8% of patients referred a perceived high frequency of information about these changes, and 54.5% believed that their opinions influenced these changes 'a great deal' or 'quite a lot.' These groups of patients overlapped notably, since up to 42.3% scored highly in both questions. Patients dissatisfied with MMT, compared to satisfied patients, reported less frequency in being informed about changes in methadone dose (3.5 (1.7) vs. 4.2 (1.4), t(63.98)=−2.37, p = 0.020) and as having significantly less influence on methadone dosage regulation (2.9 (1.3) vs. 3.5 (1.4), t(121) =−2.33, p = 0.022); although most participants had an excellent (33.3%) or mostly satisfied (35.0%) opinion of methadone as a medication for treating opioid dependence, almost a third of the participants expressed an opinion that was neither dissatisfied nor satisfied (19.5%), mostly dissatisfied (2.4%) or terrible (9.8%). There was no statistically significant difference between the dissatisfied and the satisfied with MMT groups regarding the opinion of methadone as a medication (3.6 (1.3) vs. 3.9 (1.2), t(121) =−0.97, p = 0.335).	treatment in MMT patients, as well as the first in which patient satisfaction with MMT has been evaluated in a representative sample of MMT patients of an entire region. Study participants, as a whole, reported slight satisfaction with MMT, with approximately 32% of them feeling dissatisfied. Similar scores of satisfaction have been found in two previous surveys, one carried out across in Spain. However, the percentage of dissatisfied patients was almost twice the obtained in the aforementioned studies. This marked difference could stem from the fact that patients from La Rioja might expect higher quality of services, given the high-quality level of most services available to the residents of one of the regions with a higher per capita income in Spain. Moreover, the categorical analysis of the VSSS-MT scores revealed clearly that as a whole and with basic interventions, many more patients were satisfied than dissatisfied. Percentages of satisfied and dissatisfied patients were more balanced with regard to the remaining VSSS-MT subscales, suggesting thus that specific

		interventions and social worker or psychologist skills tend to cause more divergent patient opinions than basic interventions."
Trujols et al., 2017	58.2% of participants perceived their methadone dose as inadequate (too low [4.1% of cases] or too high [54.1%]), whereas 41.8% considered their dose to be adequate (VAS-MD score=0); only the variable patient-perceived participation in methadone dosage decisions was significantly, and inversely, associated with the likelihood of perceiving methadone dose as inadequate	Patient participation in methadone dosage decisions was predictive of perceived adequacy of methadone dose beyond the contribution of multiple socio-demographic, clinical and MMT variables.

7.9 FIGURES

7.9.1 FIGURE 1. PRISMA flow diagram



7.10 SUPPLEMENTARY INFORMATION

7.10.1 S1. MEDLINE search strategy

1. (opi* adj2 addiction).mp.
2. exp Opioid-Related Disorders/
3. (opi* adj2 misuse).mp.
4. opi* abuse.mp.
5. (opi* adj1 depen*).mp.
6. exp Opiate Substitution Treatment/
7. Opioid-Related Disorder*.ti,ab.
8. Opioid disorder. ti, ab.
9. or/1–8
10. Patient Preference/
11. patient preference. ti, ab.
12. Patient Participation/
13. patient participation. ti, ab.
14. patient involvement. ti, ab.
15. patient engagement. ti, ab.
16. patient perspective. ti, ab.
17. consumer participation. ti, ab.
18. consumer engagement.ti,ab.
19. Decision Making/
20. shared decision making.ti,ab.
21. patient autonomy.ti,ab.
22. decision support.ti,ab.
23. (patient centered or patient centred).ti,ab.
24. Patient-Centered Care/
25. or/10–24

26. 9 and 25

27. limit 26 to English language