INTOLERANCE OF UNCERTAINTY DURING THE PERINATAL PERIOD

UNDERSTANDING THE ROLE OF INTOLERANCE OF UNCERTAINTY IN THE PERINATAL PERIOD: A TARGET FOR DETECTION AND PREVENTION OF ANXIETY DISORDERS DURING THE PERINATAL PERIOD

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A Thesis Submitted to the School of Graduate Studies in Partial Fulfillment of the Requirements for the Degree Doctor of Philosophy

DOCTOR OF PHILOSOPHY (2025)
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TITLE:	Understanding the role of intolerance of uncertainty in the perinatal period: A target for detection and prevention of anxiety disorders during the perinatal period
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PAGES:	xviii, 164

Lay Abstract

Anxiety disorders are common during the perinatal period, which includes both pregnancy and the postpartum period (the time following childbirth) and are associated with negative outcomes. Despite this, research focused on early detection and prevention of these disorders remains limited. Intolerance of uncertainty (IU), which refers to the tendency to react negatively to uncertain situations, is a well-established risk factor for anxiety. This dissertation explores the role of IU in improving the detection of anxiety symptoms and identifying individuals who may be at increased risk of developing anxiety disorders during the perinatal period. It also describes the development and evaluation of a psychological treatment delivered during pregnancy to reduce the risk of anxiety disorders in the postpartum period. Our research suggests that a brief questionnaire assessing IU can support early detection, and that targeting IU during pregnancy may help prevent anxiety disorders during the postpartum period. Further research into the role of IU during the perinatal period will be important for improving both the detection and prevention of anxiety disorders.

Abstract

Anxiety disorders are the most prevalent mental health disorders during pregnancy and the postpartum (perinatal) period, with prevalence rates as high as 25%. These disorders are associated with significant adverse outcomes for both the individual and their child and carry long-term costs to society. Despite this, research focused on early detection and prevention of these disorders remains limited. Intolerance of uncertainty (IU), defined as a dispositional trait that arises when an individual interprets uncertain situations as distressing, has been identified as a key risk factor in the development and maintenance of anxiety disorders in the general population, and more recently in the perinatal population. This dissertation explores the role of IU in the detection and prevention of anxiety disorders during the perinatal period. Specifically, we validated a self-report measure of IU to improve detection of anxiety disorders during the perinatal period and identify individuals who may be at increased risk for developing these disorders. We also developed and evaluated a cognitive behavioural therapy protocol targeting IU (CBT-IU) during pregnancy to reduce the risk of anxiety disorder onset in the postpartum in pregnant individuals with elevated IU. This program of research highlights the important role of IU during the perinatal period as a key target for both improving detection and prevention of anxiety disorders. We provide clinicians and researchers with a validated measure of IU to enhance detection of anxiety disorders in the perinatal period. We also offer preliminary support for CBT-IU in preventing the onset of anxiety disorders during the postpartum period, in which no participants receiving CBT-IU developed an anxiety disorder in the postpartum, compared to 31.6% who received care as usual. This dissertation emphasizes the importance of proactive strategies to enhance early detection and prevention of anxiety disorders during the perinatal period, with the potential to improve outcomes for individuals during this vulnerable period.

Acknowledgements

This research is supported by the Ontario Women's Health Scholar Award and an unrestricted educational gift from Shoppers Drug Mart (Run for Women).

I want to begin by sincerely thanking all the perinatal individuals who generously gave their time and shared their experiences. Their commitment and willingness to engage in this research will be forever appreciated, and without their contributions, this work would not have been possible.

I would like to express my sincere gratitude to my supervisors, Dr. Sheryl Green and Dr. Benicio Frey. It has been an immense honor to work alongside such inspiring clinicians and researchers whose passion and dedication to their work is truly motivating. Your exceptional mentorship, guidance, support, and wisdom have been invaluable, not only in shaping this research, but also in fostering my growth as a clinician and researcher. As I begin my career as a psychologist, I hope to carry forward the insights and guidance I have gained from your mentorship and hope to continue working alongside you both.

I would also like to sincerely thank my committee members, Dr. Randi McCabe and Dr. Louis Schmidt, for their valuable expertise and thoughtful feedback throughout the years. I deeply appreciate your ongoing encouragement, guidance, and support.

To my cohort, thank you for your support and encouragement over these many years. I'm truly grateful for the friendships we've built and the many moments we've shared, especially the laughter that carried us through the more stressful days. Going through this experience alongside you has made it all the more meaningful and memorable.

I am grateful to my friends and family for their kindness, understanding, and the joy they have brought into my life. I am so lucky to have such a wonderful support system.

To my Jackson, your unconditional love and comfort have been a constant source of calm, always bringing a smile to my face, even on the toughest days.

Finally, to my Mom, Dad, and brother Michael. There will never be enough words to fully express how grateful I am to you. Your unwavering love and support have been the foundation of who I am, and I cannot imagine who I would be or where I would be without you. You have instilled in me the values, resilience, and determination that have carried me through every step of this journey. Thank you for always encouraging me, believing in me, and providing me with every opportunity to pursue my dreams. I am truly and forever grateful.

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Chapter 2: Study One

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List of Abbreviations

AD: Anxiety disorder

AD-13: Anxiety Disorder–13 Scale

ANOVA: Analysis of variance

AUC: Area under the curve

CAD: Canadian dollar

CAU: Care as usual

CBT: Cognitive Behavioural Therapy

CBT-IU: Cognitive Behavioural Therapy for Intolerance of Uncertainty

CI: Confidence interval

CSQ: Client Satisfaction Questionnaire

DALYs: Disability adjusted life years

DERS: Difficulties in Emotion Regulation Scale

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition

DSM-5: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition

EPDS: Edinburgh Postnatal Depression Scale

EPDS-3A: Edinburgh Postnatal Depression Scale—Anxiety Subscale

FISMA: Federal Information Security Management Act

GAD: Generalized Anxiety Disorder

GAD-2: Generalized Anxiety Disorder 7-Item Scale, Abbreviated

GAD-7: Generalized Anxiety Disorder 7-Item Scale

HAM-A: Hamilton Anxiety Rating Scale

HIPAA: Health Insurance Portability and Accountability Act

HiREB: Hamilton Integrated Research Ethics Board

IPT: Interpersonal Therapy

ITT: Intention-to-treat

IU: Intolerance of Uncertainty

IUM: Intolerance of Uncertainty Model

IUS: Intolerance of Uncertainty Scale

LMM: Linear mixed model

MDD: Major Depressive Disorder

MINI: Mini International Neuropsychiatric Interview

NICU: Neonatal intensive care unit

NIH: National Institutes of Health

NCRR: National Centre for Research Resources

NPV: Negative predictive value

OCD: Obsessive-Compulsive Disorder

PASS: Perinatal Anxiety Screening Scale

PCL-5: Posttraumatic Stress Disorder Checklist for DSM-5

PPD: Postpartum depression

PPV: Positive predictive value

PSWQ: Penn State Worry Questionnaire

PTSD: Posttraumatic Stress Disorder

RCT: Randomized controlled trial

REDCap: Research Electronic Data Capture

ROC: Receiver operating characteristic

SES: Socioeconomic status

SCID: Structured Clinical Interview

SD: standard deviation

SNRI: Serotonin-norepinephrine reuptake inhibitor

SSRI: Selective serotonin reuptake inhibitor

STICSA: State-Trait Inventory for Cognitive and Somatic Anxiety

TCA: Tricyclic antidepressant

WHCC: Women's Health Concerns Clinic

YI: Youden's Index

Declaration of Academic Achievement

This dissertation comprises three studies, each of which were led by the student (M. A. Furtado), in addition to a general introduction (Chapter 1) and general discussion (Chapter 5). The student was primarily responsible for the conceptualization and design of study one, and for data collection, data analysis, and manuscript preparation. Co-authors Dr. Sheryl Green (principal investigator) and Dr. Benicio Frey (co-investigator) provided supervision throughout all stages of the project, and assisted with conceptualization, study design, and manuscript review. Study one is ***published*** in the journal **BMC Pregnancy and Childbirth.**

The student was primarily responsible for the conceptualization, study design, and manuscript preparation of study two, as well as the development of therapist and participant cognitive behavioural therapy (CBT) manuals. Co-authors Dr. Sheryl Green (principal investigator) and Dr. Benicio Frey (co-investigator) provided supervision throughout all stages of the project and contributed to the conceptualization and study design of the project, in addition to the manuscript review. Dr. Sheryl Green also contributed to the development of the CBT manuals. Co-author Dr. Randi McCabe contributed to the conceptualization of the project, provided guidance on the development of the CBT manuals, and contributed to manuscript review. Co-author Briar E. Inness contributed to the conceptualization of the project and manuscript review. Study two is ***published*** in the **Journal of Reproductive and Infant Psychology.**

The student was responsible for the conceptualization, study design, data collection, data analyses, and manuscript preparation for study three. Co-authors Dr. Sheryl Green (principal investigator) and Dr. Benicio Frey (co-investigator) provided supervision throughout all stages of the project and contributed to the conceptualization and study design of the project, in addition to

manuscript review. Co-author Dr. Randi McCabe contributed to the conceptualization of the project and manuscript review. Co-author Briar E. Inness contributed to the conceptualization of the project, data collection, and manuscript review. Study three is ***under review*** in a **peer-reviewed journal.**

Chapter 1: General Introduction

1.1 Overview

This chapter provides an overview on the prevalence and adverse consequences of anxiety disorders during pregnancy and the postpartum (perinatal) period. It explores the literature on key risk factors, existing screening tools, and current intervention approaches. The role of intolerance of uncertainty in anxiety disorders in general (non-perinatal) and perinatal populations is also discussed, with special attention placed on its potential role in improving detection and prevention of perinatal anxiety disorders. This chapter highlights that, despite the high prevalence and significant impact of anxiety during the perinatal period, systematic research on prevention strategies remains markedly limited.

1.2 Anxiety Disorders During the Perinatal Period

1.2.1 Prevalence of Anxiety Disorders During the Perinatal Period

Pregnancy and the postpartum, commonly referred to as the perinatal period, are well-known times of increased psychology vulnerability (Anderson et al., 2017; Awini et al., 2023; Giardinelli et al., 2012; Munk-Olsen & Agerbo, 2015; Womersley & Alderson, 2024). Historically, much of the scientific literature and clinical attention in perinatal mental health has focused predominantly on depression, with research on anxiety disorders during the perinatal period gaining increased recognition only in the past 15 to 20 years (Ross & McLean, 2006). Anxiety disorders during the perinatal period is now understood to be more prevalent than perinatal depression, with as many as 15 – 25% of perinatal individuals being diagnosed with an anxiety disorder during this time (Dennis et al., 2017; Fawcett et al., 2019; Roddy Mitchell et al., 2023). Among the anxiety disorders, Generalized Anxiety Disorder (GAD) is the most frequently diagnosed during the perinatal period. Recent prevalence estimates indicate that GAD affects up

to 4.1% of perinatal individuals during pregnancy and up to 5.7% during the postpartum period (Dennis et al., 2017).

1.2.2 Impact of Anxiety Disorders During the Perinatal Period

Anxiety disorders during the perinatal period are not only common but are also associated with a range of negative outcomes for both the individual and their child. Individuals with anxiety disorders during pregnancy are at greater risk of obstetric complications such as preeclampsia, preterm birth, prolonged labour and delivery, and low birth weight (Anniverno et al., 2013; Dowse et al., 2020; Hoyer et al., 2020; Qiu et al., 2009; Toscano et al., 2021; Weis et al., 2020). They are also at an increased risk of substance use disorders, recurrent mental health difficulties, and suicidality (Chin et al., 2022; Dennis et al., 2017; Orsolini et al., 2016; Pentecost et al., 2021). Anxiety disorders during the perinatal period are also associated with impaired infant bonding, which can manifest as emotional ambivalence and decreased responsive to infant cues (Göbel et al., 2018; O'Dea et al., 2023; Vagos et al., 2023). These impairments have been linked to less secure infant attachment styles and more difficult infant temperament (Davies et al., 2021; Le Bas et al., 2019). Additionally, infants of perinatal individuals with anxiety disorders are more likely to experience cognitive, emotional, and social deficits, as well as poorer attention regulation (Britton, 2011; Hennessey et al., 2023; Irwin et al., 2020; Misri et al., 2015; Rogers et al., 2020; Ross et al., 2020; Schwarze et al., 2024; Weis et al., 2020). These negative effects extend beyond infancy, with research showing that anxiety during the perinatal period is associated with poorer executive functioning (Buss et al., 2010, 2011), and an increased risk of mental health difficulties, including anxiety and depression later in life (Bernstein et al., 2005; Capron et al., 2015; Davis & Sandman, 2012; Moore et al., 2004).

The adverse outcomes associated with anxiety disorders during the perinatal period impact not only the affected individual and their children, but also impose a significant economic burden to society. Perinatal individuals with anxiety disorders are more likely to make more frequent visits to their healthcare providers (e.g., primary care providers, obstetricians) and emergency room visits, which can contribute to increased healthcare costs, placing additional strain on healthcare systems (Anniverno et al., 2013; Rubertsson et al., 2014). These individuals are more likely to take sick leave from work or work while feeling unwell, which can lead to reduced performance and long-term productivity losses in the workplace (Anniverno et al., 2013). While no direct cost estimates are currently available for anxiety disorders during the perinatal period, the annualized lifetime costs of perinatal depression in Canada are estimated at $20.6 billion CAD (Singla et al., 2023). Given that anxiety disorders are even more prevalent during the perinatal period, it is likely that the associated costs are similar, if not greater, than those of perinatal depression. The adverse developmental and emotional outcomes observed in the children of individuals with anxiety disorders during the perinatal period further contribute to increased healthcare utilization, increased demand for mental health services, and a higher need for educational supports (e.g., individualized education programs; Bauer et al., 2016; Rees et al., 2018), all of which carry long-term costs for healthcare and educational systems.

1.2.3 Risk Factors for Anxiety Disorders During the Perinatal Period

Understanding the factors that increase an individual's risk for anxiety disorders during the perinatal period is critical for early identification, intervention, and potential prevention, especially given the significant adverse outcomes associated with these disorders. When examining sociodemographic factors, low education level, specifically primary school as the highest level attained (Faisal-Cury & Rossi Menezes, 2007; Furtado et al., 2018; Martini et al.,

2015; Qiao et al., 2009), low income level (Biaggi et al., 2016; Faisal-Cury et al., 2009; Faisal-Cury & Rossi Menezes, 2007; Furtado et al., 2018), and multiparity (Furtado et al., 2018; Lederman & Weis, 2009) are associated with an increased risk of new onset anxiety disorders during the perinatal period. While some individual studies have reported associations between age and marital status with anxiety disorders during the perinatal period, meta-analyses (Bayrampour et al., 2018; Furtado et al., 2018) have not found significant associations between these sociodemographic factors and anxiety disorders during the perinatal period. Obstetrical risk factors such as a history of pregnancy loss and pregnancy medical complications (e.g., gestational diabetes, hyperemesis gravidarium) have also been shown to be associated with anxiety disorders during the perinatal period (Bayrampour et al., 2018; Bergner et al., 2008; Biaggi et al., 2016; Faisal-Cury et al., 2009; Faisal-Cury & Rossi Menezes, 2007; Gong et al., 2013).

Among psychosocial factors, inadequate support from partners, family, and/or friends has been consistently recognized as a significant risk factor for anxiety disorders during the perinatal period (Bayrampour et al., 2018; Dunkel Schetter et al., 2016; Giardinelli et al., 2012; Leach et al., 2017; Peter et al., 2017). Recent stressful life events (Karacam & Ancel, 2009; Leach et al., 2017; Yelland et al., 2010) and exposure to physical or domestic violence (Biaggi et al., 2016; Howard et al., 2013; Leach et al., 2017; Nasreen et al., 2011) have also been identified as factors increasing risk to anxiety disorders during the perinatal period.

Perhaps the most widely recognized psychological risk factor is a personal history of mood and/or anxiety disorders (Bayrampour et al., 2018; Biaggi et al., 2016; Faisal-Cury et al., 2009; Furtado et al., 2019; Giardinelli et al., 2011; Leach et al., 2017; Marchesi et al., 2014; Martini et al., 2015; Rubertsson et al., 2014). Additionally, perinatal individuals with a history of

childhood abuse are also at an increased risk of anxiety disorders during the perinatal period (Biaggi et al., 2016; Leeners et al., 2006; Martini et al., 2015; Mezey et al., 2005; Seng et al., 2014). Other psychological factors including poor subjective sleep during pregnancy (Skouteris et al., 2009; Swanson et al., 2010) and prenatal sleep disorders (Furtado et al., 2018; Qiao et al., 2009) has also been identified. Among the more recently identified psychological risk factors for anxiety worsening during the perinatal period is intolerance of uncertainty, in which individuals with high IU during pregnancy exhibit significant anxiety worsening in the postpartum (Furtado et al., 2019). The role of intolerance of uncertainty in anxiety is central to this program of research and will be explored in greater detail in the next section.

1.3 The Role of Intolerance of Uncertainty in Anxiety Disorders

Intolerance of uncertainty (IU), commonly described as a fear of the unknown (Carleton, 2016) arises when an individual interprets ambiguous or uncertain information as threatening and distressing (Carleton, 2012, 2016; Dugas et al., 1995, 1998, 2004; Freeston et al., 1994). IU is defined as a "dispositional characteristic that results from a set of negative beliefs about uncertainty and its implications" (Dugas & Robichaud, 2007, p. 24). IU involves a range of emotional, cognitive, and behavioural reactions triggered by uncertain situations. These reactions often elicit feelings of unfairness and lead to biased processing of information, causing individuals to overestimate the likelihood and severity of negative outcomes, while underestimating their ability to cope with them (Buhr & Dugas, 2006; Dugas & Robichaud, 2007; Freeston et al., 1994; Koerner & Dugas, 2006). IU was first identified and extensively researched in GAD, in which the Intolerance of Uncertainty Model (IUM) was first developed (Dugas et al., 1998). This model suggests that four main factors namely, negative beliefs about IU, positive beliefs about worry, negative problem orientation, and cognitive avoidance,

contribute to the development and maintenance of excessive and distressing worry, central to GAD.

The negative beliefs about uncertainty (e.g., uncertain situations lead to negative outcomes, negative outcomes are likely to be catastrophic) are thought to interfere with an individual's ability to effectively cope with uncertainty, leading to the use of worry as a maladaptive strategy to manage and/or prevent feared outcomes (Behar et al., 2009; Dugas et al., 1998). These individuals also hold positive beliefs about worry, such as viewing it as a positive personality trait (e.g., believing that being a worrier means they are thoughtful), and believing that worrying is an effective problem-solving strategy that can prevent negative outcomes (Freeston et al., 1994; Dugas et al., 1998).

Negative problem orientation refers to one's negative attitudes toward problems, characterized by low confidence in one's problem-solving abilities (e.g., viewing self as not being an effective problem-solver) and negative expectations about problem-solving outcomes (Dugas et al., 1995, 1997, 1998; Robichaud & Dugas, 2005; Koerner & Dugas, 2006). Lastly within the IUM, is cognitive avoidance, which is the attempt to actively avoid (e.g., thought suppression, distraction) unwanted thoughts and emotions associated with uncertainty (Dugas et al., 1998; Koerner & Dugas, 2006).

While cognitive avoidance was the only explicitly identified behavioural strategy (i.e., safety behaviour) in the IUM, continued research has identified a broader range of safety behaviours commonly associated with increased IU, such as rumination, reassurance seeking, situational avoidance, and checking (Bartoszek et al., 2022; Hebert & Dugas, 2019; Jacoby et al., 2017; Kobori & Salkovskis, 2013; Mahoney & McEvoy, 2012; Wake et al., 2022). Although these behaviours are often intended by the individual to reduce anxiety, they further reinforce

and maintain excessive and distressing worry and anxiety. Hebert and Dugas (2019) introduced a revised IUM that more explicitly highlights the role of behaviours in maintaining negative beliefs about uncertainty, as well as excessive worry and anxiety in the GAD population.

Although IU was once believed to be specific to GAD, a substantial body of research now supports IU as a transdiagnostic risk factor involved in the development and maintenance of various anxiety disorders (Carleton, 2012; Counsell et al., 2017; Dugas & Robichaud, 2007; Gentes & Ruscio, 2011; Gu et al., 2020; Morriss et al., 2023; Wilson et al., 2023), as well as other psychological disorders including obsessive-compulsive disorder (OCD; Gentes & Ruscio, 2011; Kaçar-Başaran & Gökdağ, 2025), major depressive disorder (Gentes & Ruscio, 2011; Knowles & Olatunji, 2023; Pinciotti et al., 2021), and eating disorders (Bijsterbosch et al., 2022; Kesby et al., 2019; Sternheim et al., 2017). Additionally, individuals with greater IU not only engage more frequently in maladaptive cognitive patterns (e.g., negative problem orientation), but are also more likely to experience higher levels of negative emotions (e.g., anxiety, anger, sadness) and fewer positive emotions (Morriss et al., 2023).

IU has also been identified as an important mechanism underlying CBT outcomes, particularly for disorders characterized by excessive worry and rumination. Studies have demonstrated that IU mediates the relationship between worry, negative thinking (i.e., rumination) and anxiety symptoms across anxiety disorders, OCD, and depression (McEvoy & Mahoney, 2012, 2013; Yook et al., 2010), and it has been suggested that IU may play a causal role in the maintenance of worry and anxiety (Ladouceur et al., 2000; Meeten et al., 2012). Reductions in IU have been shown to significantly mediate decreases in worry over the course of CBT, whereas changes in worry do not significantly mediate changes in IU (Bomyea et al.,

2015). Further, reductions in IU have been found to precede reductions in worry and anxiety symptoms (Goldman et al., 2007).

Given the role of IU in anxiety disorders, several CBT protocols that specifically target IU have been developed and have demonstrated strong efficacy in non-perinatal GAD populations **(**Hebert & Dugas, 2019; Dugas & Ladouceur, 2000; Robichaud, 2013; van der Heiden et al., 2012; Wilson et al., 2023; Zemestani et al., 2021). A recent meta-analysis by Wilson and colleagues (2023) found that CBT protocols specifically targeting IU in GAD populations are significantly more effective in reducing both IU and worry symptoms compared to general CBT protocols. Compared to other first-line treatments, specifically selective serotonin reuptake inhibitors, these CBT for IU protocols have been shown to produce better outcomes for treating GAD (Zemestani et al., 2021). Incorporating a specific focus on IU within CBT protocols for anxiety disorders may therefore improve treatment outcomes and may also hold promise for early interventions aimed at preventing the onset and/or worsening of worry and anxiety symptoms, such as during the perinatal period.

1.3.1 The Role of Intolerance of Uncertainty During the Perinatal Period

The perinatal period is a time of considerable change and uncertainty, involving changes in physical health, emotional well-being, social roles, responsibilities, and identity. While the role of IU has been extensively studied in relation to anxiety in general (i.e., non-perinatal) populations, its specific role during the perinatal period remains largely understudied. Research to date has identified IU as a risk factor for anxiety worsening during the postpartum (Furtado et al., 2019). Increased IU during pregnancy has also been associated with poorer psychological well-being (Çankaya & İbrahimoğlu, 2022; Çevik & Yağmur, 2018; Giurgescu et al., 2006) and fear of childbirth (Flink et al., 2023; Han et al., 2022; Rondung et al., 2019), which is itself a

known risk factor for anxiety disorders during the perinatal period. More recently, and in line with evidence in the general population, Donegan and colleagues (2022) found that reductions in IU mediated improvements in anxiety symptoms among perinatal individuals receiving CBT for anxiety disorders during the perinatal period. Although research on IU in perinatal populations is limited, findings from both perinatal and non-perinatal populations highlight the need for further study.

1.4 Screening Tools for Detecting Perinatal Anxiety and Anxiety Disorders

Despite growing recognition of perinatal anxiety and anxiety disorders and their impact, effective and early identification of symptoms remains a challenge, largely due to the limited availability of validated clinical screening tools. Among the more frequently used self-report screening tools are the Edinburgh Postnatal Depression Scale–Anxiety Subscale (EPDS–3A), the Generalized Anxiety Disorder 7-Item Scale (GAD-7), and the Perinatal Anxiety Screening Scale (PASS).

The EPDS is a gold-standard 10-item self-report questionnaire used widely for screening perinatal depression (Cox et al., 1987). Factor analyses have identified three EPDS items that cluster on an anxiety factor, leading to the development of the anxiety subscale the EPDS–3A (Bina & Harrington, 2016; Jomeen & Martin, 2005). Phillips and colleagues (2009) found a cut-off score of 4 or greater, resulting in a sensitivity of 63% and specificity of 70% for detecting an anxiety disorder in the perinatal period. Alternatively, Matthey and colleagues (2008) suggest an optimal cut-off score of 6 or greater, with a sensitivity of 66.7% and specificity of 88.2%. Other researchers (Fairbrother et al., 2019; Marsay et al., 2017; van Heyningen et al., 2018) have suggested that the EPDS–3A does not perform well enough to be used as a screening tool for detection of an anxiety disorder during the perinatal period, as it results in a high rate of false

positives and does not meet the recommended threshold (AUC ≥ 0.70 and a Youden's index of ≥ 0.40) to demonstrate evidence of accuracy.

The GAD-7 is a widely used self-report measure of general anxiety symptoms (Spitzer et al., 2006) and has been validated for use in the postpartum period (Simpson et al., 2014). Simpson and colleagues (2014) suggest an optimal cut-off score of 13 or greater in detecting the presence of GAD in the postpartum, yielding a sensitivity of 61.3% and specificity of 72.7%. While the GAD-7 has demonstrated evidence of screening accuracy for anxiety disorders during the perinatal period, with reported AUC values of 0.78 (Fairbrother et al., 2019) and 0.82 (Austin et al., 2022), concerns about its limitations in sensitivity have also been raised (Fairbrother et al., 2019).

Unlike the EPDS–3A and GAD-7, the PASS is a 31-item self-report questionnaire that was designed specifically to screen for perinatal individuals who may be at increased risk of clinically significant anxiety symptoms (Somerville et al., 2014). A clinical cut-off score of 26 or higher on the PASS has been recommended to distinguish between perinatal individuals at high versus low risk for an anxiety disorder (Koukopoulous et al., 2021; Yazıcı et al., 2019). Of note however, the PASS was designed based on DSM-IV criteria for anxiety disorders, which included obsessive-compulsive disorder and post-traumatic stress disorder.

1.5 Treatment Approaches for Anxiety Disorders During the Perinatal Period

Various treatment approaches for increased anxiety and anxiety disorders during the perinatal period have been developed and evaluated. The Canadian Network for Mood and Anxiety Treatments (CANMAT) guidelines provides the most recent Canadian treatment guidelines, which organizes treatment recommendations by intervention intensity, ranging from low-intensity interventions (e.g., lifestyle interventions) to higher-intensity options (e.g.,

psychological therapies, pharmacotherapy). To maintain consistency, this section follows the same organizational framework as the CANMAT guidelines.

When evaluating lifestyle interventions, exercise programs have demonstrated second-line effectiveness (Vigod et al., 2025). Specifically, these programs have been shown to reduce anxiety symptom severity during pregnancy, with greater effects being seen when the program was group-based (Sánchez-Polán et al., 2021; Vigod et al., 2025). Sleep protection interventions, such as CBT for insomnia, have also demonstrated effectiveness at reducing anxiety symptoms in pregnancy, in addition to improvements in sleep quality (Vigod et al., 2025). As inadequate social support is a well-established risk factor for increased anxiety and anxiety disorders during the perinatal period, psychosocial interventions such as peer support, have been investigated. These interventions have demonstrated some effectiveness as a second-line treatment for reducing anxiety symptoms during the perinatal period (Sufredini et al., 2022), however, further research in this area is needed, particularly in perinatal individuals with anxiety disorders.

Psychological treatments are recommended as a first-line option for perinatal individuals with moderate anxiety symptom severity, or for those with mild symptoms when lifestyle or psychosocial interventions are ineffective or inaccessible (Vigod et al., 2025). CBT and mindfulness-based treatments have demonstrated the strongest efficacy for reducing anxiety symptoms and treating perinatal individuals with anxiety disorders (Clinkscales et al., 2023; Leng et al., 2023; Webb et al., 2021; Zimmerman et al., 2023). These psychological treatments have demonstrated effectiveness in both individual and group formats, as well as when delivered in-person or virtually. Additionally, guided self-help psychological interventions are recommended as a second-line treatment for reducing anxiety symptom severity during the perinatal period (Bayrampour et al., 2019; Ching et al., 2023; Evans et al., 2022; Chae et al.,

2021), with some evidence of guided internet-based CBT in pregnancy as a third-line treatment for fear of childbirth (Evans et al., 2022), a known risk factor for anxiety disorders during the perinatal period. Pharmacological interventions are commonly used when symptoms are more severe, or for individuals with milder symptom severity but who either cannot access psychological interventions, or prefer pharmacotherapy (Vigod et al., 2025). Antidepressants are considered first-line medications for anxiety disorders in the general population, however, there are no RCTs evaluating the effectiveness of these medications for anxiety disorders in the perinatal period specifically (Vigod et al., 2025). Most studies evaluating the safety of antidepressants during the perinatal period have focused on selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants, and safety data have been reasonably reassuring (Vigod et al., 2025).

1.6 Current Approaches to Preventing Anxiety Disorders During the Perinatal Period

Although numerous effective interventions have been developed to treat anxiety disorders during the perinatal period after symptom onset, efforts to prevent the onset of anxiety disorders remain significantly limited. Despite the well-known consequences of anxiety disorders during the perinatal period, prevention has received far less attention than other areas of perinatal mental health, particularly when compared to efforts made in preventing postpartum depression. Psychosocial interventions, specifically trained peer support, has been recommended as a first-line preventative treatment for postpartum depression (O'Connor et al., 2019; Vigod et al., 2025). Among psychological approaches, CBT and interpersonal therapy (IPT) are recommended as first-line prevention strategies for postpartum depression, supported by the highest level of evidence (Force USPST et al., 2019; O'Connor et al., 2019; Vigod et al., 2025). Guided self-help psychological interventions are recommended as second-line options (Vigod et

al., 2025). Notably, all strategies shown to be effective in preventing postpartum depression have been implemented with perinatal individuals identified as high risk, either due to the presence of established risk factors (e.g., history of mood disorders, low socioeconomic status) or subsyndromal symptoms. This highlights the importance of identifying individuals at increased risk for anxiety disorders during the perinatal period and using that information to inform the development and implementation of prevention strategies aimed at reducing the likelihood of anxiety disorder onset and related adverse outcomes.

While prevention efforts for postpartum depression have made considerable progress, research specifically addressing prevention of anxiety disorders during the perinatal period remains extremely limited. Guided self-help interventions (Milgrom et al., 2011; O'Mahen et al., 2014; Trevillion et al., 2020) have shown some potential in preventing anxiety worsening among perinatal individuals at increased risk (i.e., those with established risk factors and/or subclinical symptoms). These findings, however, are drawn from studies targeting the prevention of postpartum depression, in which increased anxiety symptoms and disorders during the perinatal period were not the primary outcome and often not assessed with diagnostic interviews to confirm diagnoses. Collectively, these very limited findings point to a significant gap in the literature regarding the prevention of anxiety disorders during the perinatal period. Most existing studies lack a direct focus on the prevention of anxiety disorders during the perinatal period specifically, with anxiety frequently examined as a secondary outcome in postpartum depression research and typically assessed through self-report measures rather than diagnostic assessment. As such, there remains a critical need for prevention efforts specifically focused on anxiety disorders during the perinatal period that use existing knowledge of risk factors to guide the development of effective, evidence-based strategies.

1.7 Conclusions and Aims of Current Research Program

Anxiety disorders during the perinatal period are both prevalent and significantly impacting, affecting the perinatal individual, their offspring, and society. Despite considerable progress in identifying key risk factors, research validating tools to effectively identify perinatal individuals at risk for anxiety disorders based on these factors remains limited. While IU is a well-established risk factor in non-perinatal anxiety, and recently recognized as a risk factor for anxiety worsening during the postpartum period, its role during the perinatal period remains underexplored, both in enhancing detection and as a potential target for prevention. Accordingly, the current program of research aims to evaluate whether IU can be used both to improve detection of perinatal individuals at risk for anxiety disorders and as a modifiable target to prevent the onset of these disorders during the postpartum period.

First, we were interested in determining whether assessing IU could improve the detection of anxiety disorders during the perinatal period and identify individuals at increased risk of such disorders. In Study One (Chapter 2) we sought to validate the Intolerance of Uncertainty Scale, a commonly used self-report measure assessing IU, for use in the perinatal population. We evaluated the psychometric properties of the IUS and assessed whether an optimal clinical cut-off score could enhance the identification of those at risk for anxiety disorders during the perinatal period. This study contributes to the limited literature on validated screening tools for anxiety disorders during the perinatal period.

Second, buildings on our findings from Study One, we aimed to develop a targeted CBT protocol for individuals at increased risk of developing anxiety disorders during the perinatal period. In Study Two (Chapter 3) we outline the study protocol for a proof-of-concept randomized controlled trial designed to evaluate this novel CBT protocol, which specifically

targets IU during pregnancy in individuals identified as *high risk*, as informed by our Study One findings. This study details the study procedures and development of the CBT for IU protocol in preparation for evaluating its potential preventative impact in Study Three (Chapter 4).

Third, we evaluated the effectiveness of the protocol developed in Study Two. In Study Three (Chapter 4), we present the findings from the proof-of-concept randomized controlled trial comparing CBT for IU to care as usual in preventing the onset of anxiety disorders in the postpartum period. The results from this study add to the very limited literature on preventative approaches for anxiety disorders in the perinatal period and highlight the potential of IU as a modifiable target for prevention.

Finally, Chapter 5 provides a general discussion of these studies and highlights how they advance our understanding of the role of IU during the perinatal period in both improving anxiety detection and serving as a promising target for prevention. This chapter also addresses the limitations, significance, and future directions of this research. Taken together, this program of research highlights the importance of proactive and prevention focused approaches to improve outcomes for perinatal individuals.

Chapter 2: Study One

Validation of the intolerance of uncertainty scale as a screening tool for perinatal anxiety

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Furtado, M., Frey, B. N., & Green, S. M. (2021). Validation of the intolerance of uncertainty scale as a screening tool for perinatal anxiety. *BMC Pregnancy and Childbirth, 21*(1), 829. https://doi.org/10.1186/s12884-021-04296-1

2.1 Abstract

Background: To date, there is a significant lack of research validating clinical tools for early and accurate detection of anxiety disorders in perinatal populations. Intolerance of uncertainty was recently identified as a significant risk factor for postpartum anxiety symptoms and is a key trait of non-perinatal anxiety disorders. The present study aimed to validate the Intolerance of Uncertainty Scale (IUS) in a perinatal population and evaluate its use as a screening tool for anxiety disorders.

Methods: Psychiatric diagnoses were assessed in a sample of perinatal women (n=198), in addition to completing a self-report battery of questionnaires. Psychometric properties including internal consistency and convergent and discriminant validity were assessed. Determination of an optimal clinical cut-off score was measured through a ROC analysis in which the area under the curve, sensitivity, specificity, as well as positive and negative predictive values were calculated.

Results: The IUS demonstrated excellent internal consistency (α=0.95) and an optimal clinical cut-off score of 64 or greater was established, yielding a sensitivity of 89%. The IUS also demonstrated very good positive (79%) and negative (80%) predictive values.

Conclusions: These findings suggest that the IUS represents a clinically useful screening tool to be used as an aid for the early and accurate detection of perinatal anxiety.

Keywords: anxiety; perinatal; pregnancy; postpartum; screening; intolerance of uncertainty

2.2 Background

As many as 1 in 4 individuals globally are diagnosed with an anxiety disorder in their lifetime, in which women are twice as likely to be diagnosed compared to men (Remes et al., 2016). Women account for approximately 65% of the 26.8 million disability adjusted life years (DALYs) (Baxter et al., 2014; Whiteford et al., 2013) and anxiety disorders are associated with substantial economic burden. Anxiety, together with depression, accounts for over $1 trillion per year in healthcare and lost productivity (Chisholm et al., 2016), with anxiety disorders in Canada alone costing the economy $17.3 billion per year (Conference Board of Canada, 2016).

Until recently, perinatal mental health research has focused on postpartum depression (PPD) which affects as many as 12% of women (Shorey et al., 2018), however, there has been increasing awareness that the perinatal period is also associated with high risk for anxiety disorders. In fact, anxiety disorders during the perinatal period have been shown to be more prevalent than PPD, with rates between 15-24% (Dennis et al., 2017). Further, numerous negative effects are associated with perinatal anxiety disorders for both mothers and their infants. For instance, in addition to the distress and impairment associated with an anxiety disorder, anxiety during pregnancy has been associated with increased obstetric complications such as preterm birth and lower birth weight (Anniverno et al., 2013; Grigoriadis et al., 2018; Kramer et al., 2009; Orr et al., 2007). Women with perinatal anxiety utilize greater health resources, such as making more frequent visits to their obstetrician (Andersson et al., 2014; Rubertsson et al., 2014) and have increased absenteeism from work because of their anxiety (Anniverno et al., 2013). These negative effects also impact the mother-infant bond, such that women are more likely to report reduced perceived bonding with their infant (Tietz et al., 2014). Infants of mothers with perinatal anxiety experience greater cognitive and attention difficulties (Davis & Sandman, 2010;

Huizink et al., 2002) and are more likely to experience their own anxiety later in life (Bernstein et al., 2005; Capron et al., 2015; Davis & Sandman, 2012). Despite the high prevalence rates of perinatal anxiety disorders and associated negative effects, less than 15% of women receive appropriate treatment (Smith et al., 2009), often due to difficulties in timely and accurate symptom detection.

A lifetime history of mood and/or anxiety disorders are among the strongest predictors of perinatal anxiety (Rubertsson et al., 2014; Faisal-Cury et al., 2009; Martini et al., 2015). Sociodemographic risk factors on the other hand, such as maternal age, parity, and education level, have demonstrated inconsistent findings in the literature (Bayrampour et al., 2012; Biaggi et al., 2016; Tearne et al., 2016; Yelland et al., 2010). More recently, a key trait of anxiety disorders known as intolerance of uncertainty, was identified as a significant risk factor for postpartum anxiety worsening in women with pre-existing anxiety disorders (Furtado et al., 2019). Intolerance of uncertainty results from negative beliefs about uncertainty and its potential negative implications (Buhr & Dugas, 2009). Intolerance of uncertainty is any type of emotional, cognitive, and/or behavioural response to uncertainty which biases information processing, resulting in perceived negative implications (Freeston et al., 1994). It is a common characteristic across anxiety disorders (Boswell et al., 2013; Buhr & Dugas, 2002; McEvoy & Mahoney, 2011; Wright et al., 2016) and is positively correlated with worry symptoms (Counsell et al., 2017; Dugas et al., 2001; Yook et al., 2010). Further, intolerance of uncertainty has been demonstrated as a significant predictor and mediator of treatment response to cognitive behavioural therapy in non-perinatal populations (Bomyea et al., 2015).

To date, there is a paucity of research validating clinical tools for anxiety disorders in perinatal populations. Among self-report screening tools for perinatal anxiety are the Edinburgh

Postnatal Depression Scale (EPDS), the Generalized Anxiety Disorder 7-Item Scale (GAD-7), the Perinatal Anxiety Screening Scale (PASS) and the Anxiety Disorder−13 Scale (AD−13). Although the EPDS is a well-validated screening tool for PPD (Cox et al., 1987; Levis et al., 2020) and has been used as a multidimensional tool (EPDS−3A) to screen for perinatal anxiety, it is associated with a high rate of false positives (Matthey et al., 2013) and is not recommended for widespread use as a screening tool for perinatal anxiety disorders (Fairbrother et al., 2019). The GAD-7 is one of the most commonly used self-report questionnaires in assessing anxiety symptom severity in the general population (Spitzer et al., 2006) and has been validated for use in the perinatal period (Simpson et al., 2014). Although the GAD-7, and the abbreviated GAD-2, perform slightly better than the EPDS−3A in detecting symptoms of GAD in perinatal women, they too, have not been recommended as a perinatal anxiety disorder screening tool for widespread use Fairbrother et al., 2019). Unlike the EPDS and GAD-7, the PASS (Somerville et al., 2014) was specifically designed to screen for a broad range of anxiety symptoms during pregnancy and the postpartum. Utilizing the validated clinical cut-off score of 26 or greater, the PASS has demonstrated fair accuracy (68%) in identifying perinatal women with an anxiety diagnosis compared to the EPDS−3A and GAD-7 (Somerville et al., 2014). Psychiatric diagnoses in this study, however, were not confirmed through the use of a standardized psychiatric interview (e.g., MINI, SCID), which may have limited the accuracy of diagnoses. The AD−13, which identifies core symptoms of anxiety disorders, has been found to better perform at accurately identifying anxiety disorders during the perinatal period (Fairbrother et al., 2019). Of note however, the AD−13 includes questions assessing Obsessive-Compulsive Disorder and Posttraumatic Stress Disorder, which are not currently considered anxiety

disorders, as per the Diagnostic and Statistical Manual of Mental Disorders (Fairbrother et al., 2019).

Given that intolerance of uncertainty has been well-documented as a risk factor for anxiety disorders in the general population and more recently in a perinatal population and shown to be a significant predictor of treatment response, it would be of great value to validate the IUS as a clinical tool for perinatal anxiety disorder screening. The 27-item Intolerance of Uncertainty Scale (IUS) is among the most commonly utilized and validated self-report questionnaire assessing intolerance of uncertainty. Therefore, the objective of the present study was to validate the psychometric properties of the IUS as a screening tool for clinical anxiety disorders in pregnant and postpartum women. Further, as clinical cut-off scores can be especially beneficial in screening for psychiatric disorders, we examined whether an optimal cut-off score could be achieved for detection of an anxiety disorder during the perinatal period. We hypothesized that the IUS would display high validity and reliability in detecting the presence of an anxiety disorder during the perinatal period. We further hypothesized that a cut-off with high sensitivity and predictive value would be determined in predicting the presence of an anxiety disorder during the perinatal period.

2.3 Methods

2.3.1 Participants and Procedures

Pregnant (≥14 weeks gestation) and postpartum (≤6 months) women, 18 years or older were enrolled in the present study. As the first trimester of pregnancy is associated with highest medical risk and in turn, understandable levels of anxiety, participants were recruited beginning in their second trimester of pregnancy to better identify those who would be more likely to experience anxiety symptoms which would persist. The time interval used to determine the

postpartum period differs among studies and may be as high as 12 months postpartum (Britton et al., 2008). Given that the prevalence rates of anxiety disorders are highest by 6 months postpartum (Dennis et al., 2017; Yelland et al., 2010; Britton, 2008; Wenzel et al., 2003, 2005), the present study utilized these criteria to define the postpartum period. Participants were recruited from the Women's Health Concerns Clinic at St. Joseph's Healthcare Hamilton, an outpatient mental healthcare clinic, prior to receiving psychological treatment (Caropreso et al., 2020). Participants were also recruited through advertising in midwifery, physician clinics, and online (e.g., Kijiji) throughout the Greater Toronto and Hamilton area, between January 2020 to February 2021. Once eligibility was determined, participants completed a research study visit in which psychiatric diagnoses were assessed by the Mini International Neuropsychiatric Interview (MINI), version 7.0.2 for the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). Upon completion of the study visit, participants were divided into two cohorts for analyses: those with a DSM-5 primary anxiety disorder and those without. Co-morbid secondary conditions were accepted for both cohorts so that the results of the study resemble what is observed in the real-world.

In addition to the MINI, participants completed a battery of self-report questionnaires *(see Study Measures below)* assessing clinical symptom severity of anxiety, worry, mood, and emotion regulation. To assess test-retest reliability, participants who agreed to participate in a second study visit, repeated the self-report questionnaire battery two-weeks after completion of their initial study visit. Study data was electronically stored and managed with the Research Electronic Data Capture (REDCap) system, which is a secure web-based application designed for research data collection (Harris et al., 2009). This study was conducted in accordance with

the Declaration of Helsinki and was approved by the Hamilton Integrated Research Ethics Board. All participants provided written informed consent.

2.3.2 Study Measures

A brief demographics questionnaire was included in the battery of self-report questionnaires administered to participants. The demographics questionnaire included questions pertaining to the participant's age, perinatal status, ethnicity, marital status, parity, education level, and medical history (e.g., medication use).

The *Intolerance of Uncertainty Scale (IUS)* is a 27-item self-administered questionnaire assessing one's beliefs and reactions to uncertain events, ambiguity, and the future (Buhr & Dugas, 2002; Freeston et al., 1994). Items are scored on a 5-point Likert scale, ranging from 1 (not at all characteristic of me) to 5 (entirely characteristic of me), with total possible scores of 27 to 135. Although initial validation studies have established a multifactorial structure, scores are most often reported as a total scale score. The IUS has demonstrated excellent internal consistency (α=0.91-0.95) and good test-retest reliability (r=0.78) in general (non-perinatal) populations.

The *Generalized Anxiety Disorder 7-Item Scale (GAD-7)* is a 7-item self-report questionnaire assessing anxiety symptom severity for the previous two-week period (Spitzer et al., 2006). Items on the GAD-7 are measured on a 4-point Likert scale ranging from 0 (not at all) to 3 (nearly every day). The GAD-7 has good sensitivity (89%) and specificity (82%) in detecting a clinical diagnosis of GAD, when a cut-off score of 10 or higher is utilized. The GAD-7 has also been validated in a perinatal population, yielding adequate sensitivity (61.3%) and specificity (72.7%) with an optimal cut-off score of 13 or higher (Simpson et al., 2014).

The *Edinburgh Postnatal Depression Scale (EPDS)* is a 10-item self-report questionnaire assessing perinatal depression (Cox et al., 1987). Items are scored on a 4-point Likert scale, with higher scores indicating greater depressive symptom severity. The EPDS has demonstrated good sensitivity and specificity at 86% and 78%, respectively, for a diagnosis of Major Depressive Disorder when a clinical cut-off score of 10 or higher is utilized. Recent studies, however, have demonstrated a cut-off score of 13 or higher for the detection of postpartum depression specifically (Matthey et al., 2006). The EPDS has also been used to assess postpartum anxiety, with 3 of the 10 included questions specifically probing into anxiety symptoms Matthey et al., 2013).

The *Penn State Worry Questionnaire (PSWQ)* is a 16-item self-administered questionnaire assessing worry symptoms (Meyer et al., 1990). Items are scored on a 5-point Likert scale, ranging from 1 (not at all typical of me) to 5 (very typical of me), with scores at or above 65 representing a clinically significant level of worry (Fresco et al., 2003). The PSWQ has been considered a gold-standard for assessing worry and has demonstrated excellent psychometric properties in both perinatal and non-perinatal population (Blackmore et al., 2016; Swanson et al., 2011; Zhong et al., 2009).

The *State-Trait Inventory for Cognitive and Somatic Anxiety (STICSA)* consists of two 21-item self-report subscales assessing state and trait anxiety (Ree et al., 2008). The "state" subscale assesses the individuals current, *at this very moment*, anxiety, while the "trait" subscale refers to how individuals feel *in general.* For the purposes of the present study, the trait subscale was utilized. Items are scored on a 4-point Likert scale ranging from 1 (not at all) to 4 (very much so). The STICSA can be scored to assess cognitive anxiety symptoms (e.g., rumination, intrusive thoughts) and somatic anxiety symptoms (e.g., dizziness, sweating, heart racing)

separately. The STICSA has demonstrated excellent validity and reliability (Grös et al., 2007). To detect the presence of a clinical anxiety disorder, a cut-off score of 43 or higher has been suggested (Van Dam et al., 2013).

The *Difficulties in Emotion Regulation Scale (DERS)* is a 36-item self-report questionnaire assessing six dimensions of emotion regulation: non-acceptance, goals, impulse, awareness, strategies, and clarity (Gratz et al., 2004). Items on scored on a 5-point Likert scale ranging from 1 (almost never, 0-10%) to 5 (almost always, 91-100%), with higher scores indicating greater difficulties in regulating one's emotions. The DERS has demonstrated good internal consistency and test-retest reliability (Hallion et al., 2018).

2.3.3 Statistical Analyses

Independent samples t-tests were performed to compare continuous variables (e.g., age) between participants with and without a primary anxiety disorder. Chi-square tests were utilized to assess group differences for categorical data (e.g., parity). Reliability of the IUS was assessed by measuring internal consistency using Cronbach's alpha and with test-retest reliability. To assess convergent and discriminant validity, correlations with well-established measures of worry, anxiety, depression, and emotion regulation were measured. To assess criterion validity, a receiver operating characteristic (ROC) analysis was utilized to estimate the sensitivity and specificity pairings, the area under the curve (AUC) and 95% confidence interval (CI) for a range of cut-off scores for the IUS. The AUC was used to determine the screening accuracy of the IUS in predicting a primary anxiety disorder during the perinatal period. The optimal clinical cut-off score of the IUS was set by the largest Youden Index (YI), which is derived from the sum of sensitivity and specificity minus one. Based upon the optimal clinical cut-off of the IUS, as determined by the YI, sensitivity, specificity, positive (PPV) and negative (NPV) predictive

values were calculated. To confirm the accuracy and specificity of the IUS as an anxiety disorder screening tool during the perinatal period, an ROC analysis, calculation of an optimal cut-off score and associated sensitivity, specificity, PPV and NPV were calculated to also assess the use of the IUS as a screening tool for primary and/or secondary depressive disorders (e.g., Major Depressive Disorder, Persistent Depressive Disorder). The level of statistical significance was set at a p-value < 0.05. All statistical analyses were performed with IBM SPSS Statistics 23 (IBM Corp., 2015).

2.4 Results

Pregnant (n=92) and postpartum (n=106) women meeting all inclusion/exclusion criteria were enrolled in the present study, for a total of 198 participants. Participants ranged in age from 19 to 44 years, with a mean age of 31.8 years (SD=4.37). In assessing current psychiatric diagnoses, as per the MINI for DSM-5, 118 participants met criteria for a primary anxiety disorder and 80 participants did not. The most common primary anxiety disorder was GAD (89.8%), followed by Social Anxiety Disorder (5.9%) and Panic Disorder (4.2%). Of the 80 participants without a primary anxiety disorder, 51.2% did not meet criteria for any lifetime psychiatric disorders, 22.5% had past Major Depressive Disorder (MDD), while 5% had current MDD. Baseline characteristics for participants are outlined in **Table 1**.

Table 1. Baseline demographics and characteristics (n=198)

	Primary AD (n=118)	**Control (n=80)**	**p-value**
Mean age (SD)	31.1 (4.57)	32.8 (3.85)	0.07
Perinatal Status			
Pregnant	47 (39.8%)	45 (56.2%)	0.02
Postpartum	71 (60.2%)	35 (43.8%)	

Ethnicity			
Caucasian	98 (83.1%)	60 (75%)	
Black	2 (1.7%)	0 (0%)	
First Nations	2 (1.7%)	0 (0%)	
Latino/Hispanic	1 (0.9%)	2 (2.5%)	0.05
Middle Eastern	1 (0.9%)	3 (3.8%)	
South Asian[a]	0 (0%)	3 (3.8%)	
East Asian[b]	0 (0%)	3 (3.8%)	
Asian/Pacific Islander	4 (3.4%)	1 (1.2%)	
Other	10 (8.5%)	8 (10%)	
Marital Status			
Single	6 (5.1%)	1 (1.2%)	0.14
Married/Common-law	111 (94.1%)	76 (95%)	
Divorced	1 (0.8%)	3 (3.8%)	
Parity			
Primigravida	81 (68.6%)	47 (58.8%)	0.15
Multigravida	37 (31.4%)	33 (41.2%)	
Education			
≤High school	12 (10.2%)	9 (11.2%)	
College/University[c]	87 (73.7%)	41 (51.2%)	0.002
Postgraduate (e.g., MD, PhD)[d]	19 (16.1%)	30 (37.5%)	

Post-hoc analyses for chi-square tests revealed statistically significant differences between the primary AD and control groups in ethnicity ([a]South Asian, [b]East Asian) and education level ([c]College/University and [d]Postgraduate).

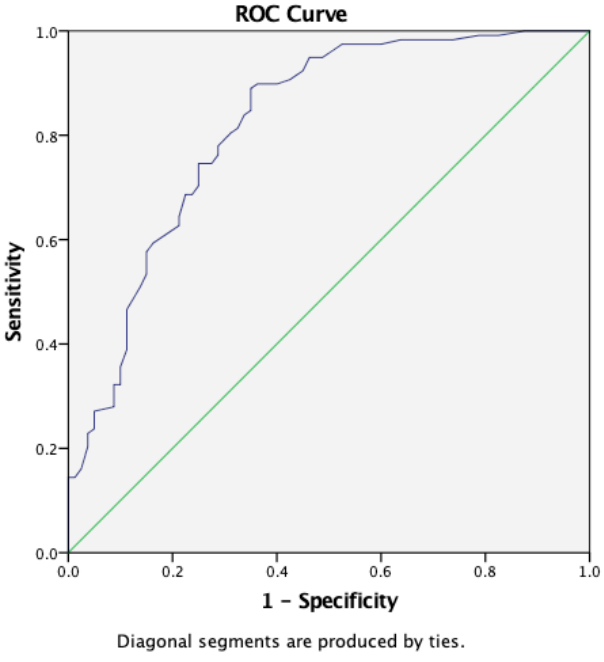
2.4.1 Reliability and Validity

The IUS demonstrated excellent internal consistency (α=0.95) in the present sample. To assess test-retest reliability, a sample of participants (n=35) repeated the study measures two weeks after their baseline assessment. In test-retest analysis, the correlation between baseline and follow-up IUS scores was excellent (r=0.91). To assess convergent and discriminant validity, Pearson correlations between IUS scores and included self-report measures was examined. Further convergent validity was demonstrated between the IUS and PSWQ (r= 0.75, p<0.001), GAD-7 (r=0.73, p<0.001), STICSA total scale (r=0.74, p<0.001) and cognitive subscale (r=0.79, p<0.001), and DERS (r=0.74, p<0.001). Although all correlations were statistically significant, the strength of correlations between the IUS and EPDS depression subscale (r=0.55, p<0.001) and STICSA somatic subscale (r=0.53, p<0.001) were considered moderate demonstrating discriminant validity.

2.4.2 Diagnostic Accuracy

The ROC curve for the IUS is illustrated in **Figure 1**. The AUC was calculated to examine the performance of the IUS as a screening tool in detecting the presence of an anxiety disorder in perinatal women. Accuracy was interpreted as having low (AUC= 0.50 to 0.70), acceptable (AUC= 0.70 to 0.80), excellent (AUC= 0.80 to 0.90), and outstanding (AUC= 0.90 or greater) discrimination (Hosmer & Lemeshow, 2000). The AUC of the IUS was calculated as 0.82 (95% CI: 0.76-0.88), indicating that the IUS had excellent screening accuracy for primary anxiety disorders among perinatal women. When maximizing the Youden Index (YI=0.54), an optimal clinical cut-off score of 64 was found. Sensitivity and specificity at the optimal clinical cut-off score of 64 or greater was 89% and 65%, respectively. Further, the IUS demonstrated very good PPV (79%) and NPV (80%).

Figure 1. Receiver operating characteristic (ROC) curve for the IUS to detect primary anxiety disorders during the perinatal period.



In assessing the use of the IUS as a depression screening tool during the perinatal period, the AUC was calculated as 0.59 (95% CI: 0.51-0.69), indicating low discrimination. When maximizing the Youden Index (YI=0.24, interpreted as low), an optimal clinical cut-off score of 76 was found. Sensitivity and specificity at the optimal clinical cut-off score of 76 or greater was 69% and 55%, respectively. Further, the IUS demonstrated good NPV (87%), however very poor PPV (27%) in predicting the presence of a depressive disorder during the perinatal period.

2.5 Discussion

Anxiety disorders during the perinatal period are highly prevalent and are associated with significant burden and negative outcomes for both mother and child. Unlike other disorders such as perinatal depression, there are very few screening tools which have been validated for use in perinatal anxiety. Further, the screening tools which have been validated in a perinatal

population have demonstrated high false positive rates and are not recommended for widespread use in screening of perinatal anxiety disorders.

This was the first study to specifically examine the use of the IUS as a screening tool for perinatal anxiety disorders. Previous research has demonstrated the importance of intolerance of uncertainty in anxiety disorders both in the general population (Boswell et al., 2013; Buhr & Dugas, 2002; McEvoy & Mahoney, 2011; Wright et al., 2016; Counsell et al., 2017; Dugas et al., 2001; Yook et al., 2010), and more recently in the perinatal population (Furtado et al., 2019) in which higher scores were associated with postpartum anxiety worsening. Overall, the current results support the use of the IUS as a potential screening tool for perinatal anxiety disorders. The 27-item IUS demonstrated excellent internal consistency and test-retest reliability among our sample of pregnant and postpartum women. The IUS was also positively correlated with measures of anxiety and worry, demonstrating convergent validity. Of note, the IUS was correlated with STICSA total scores and cognitive subscale scores, but less so with somatic subscale scores. Given that intolerance of uncertainty is defined as a cognitive bias impacting the way one perceives, interprets, and responds to uncertain events, it is understandable as to why the IUS would not be strongly correlated to somatic anxiety symptoms (e.g., heart racing), which demonstrates discriminant validity. Similarly, the IUS demonstrated convergent validity with the DERS, which is a measure of emotion dysregulation. Individuals with anxiety disorders exhibit strong emotional reactions and often have difficulties interpreting their emotions, which can further exacerbate their worry and use of maladaptive coping behaviours (Kashdan et al., 2008; Mennin et al., 2005, 2007; Tull et al., 2008; Ouellet et al., 2019). Further, intolerance of uncertainty has been known to contribute to worry via negative problem orientation. Individuals high in intolerance of uncertainty tend to exhibit pessimistic views towards any potential

problem or uncertain situations, perceiving them as threats and, in turn, doubting their abilities to cope with or resolve them if needed (Ouellet et al., 2019). Due to this negative problem orientation, these individuals will often avoid any uncertain situation reinforcing their cognitive biases and producing anxiety and emotional distress (Dugas et al., 2004; Gosselin et al., 2005). Recent research has also revealed that emotion dysregulation is significantly associated with anxiety symptoms during pregnancy (Lin et al., 2019) and is a significant mediator of the relationship between intolerance of uncertainty and worry in a non-perinatal population (Ouellet et al., 2019). As emotional states are intrinsically linked to uncertainty, and given the relationship between emotion dysregulation and anxiety, it is understandable as to why convergent validity was exhibited between the IUS and DERS.

The present study also demonstrated discriminant validity between the IUS and EPDS, particularly the EPDS depression subscale which removes the three anxiety items. Although the correlation between these measures were significant, the relationship was moderate therefore supporting discriminant validity. Perinatal anxiety and depressive disorders are highly comorbid (Dikmen-Yildiz et al., 2017; Field et al., 2010; Hirschfield, 2001; Zhou et al., 2017) and overlapping symptomatology may even hinder accurate symptom detection (Dennis et al., 2017). Limited research has also demonstrated the association between intolerance of uncertainty and depressive symptomatology, suggesting that high intolerance of uncertainty may be a risk factor for the development of depression (Dar et al., 2017; Saulnier et al., 2019). The findings however have been robust in nature and require further investigation. As intolerance of uncertainty and depression are associated, it is reasonable as to why the IUS, a key trait in anxiety disorders, would be significantly correlated with the EPDS. Nevertheless, the correlation was to a moderate degree, as the items on the EPDS assess distinctive depressive symptoms such as anhedonia,

hopelessness, and self-injurious behaviour, which are not always exhibited in anxiety disorders. Further, in assessing the use of the IUS as a screening tool for depressive disorders during the perinatal period, the IUS demonstrated poor screening accuracy (AUC=0.59). These results suggest that although intolerance of uncertainty has been found to be associated with depression, it is not a good screening tool to detect the presence of depressive disorders during the perinatal period. Instead, the results suggest the specificity of the IUS in screening for anxiety disorders during the perinatal period and other validated screening tools such as the EPDS are suggested for depressive disorder screening.

The accuracy of the IUS as a screening tool, as assessed by the AUC, was interpreted as excellent at 0.82. The AUC of the IUS in this study is greater than those measures (e.g., EPDS-3A, GAD-7) which are commonly used as screening tools for perinatal anxiety (Fairbrother et al., 2019; Simpson et al., 2014; van Heynigen et al., 2018). Sensitivity of the IUS in detecting a primary perinatal anxiety disorder was excellent, while specificity was fair. When validating a measure to be utilized in clinical populations as a screening tool, positive and negative predictive values are considered more relevant than sensitivity and specificity (Trevethan, 2017). Higher NPV and PPV values are recommended to demonstrate accuracy in screening detection (Fairbrother et al., 2019; Trevethan, 2017). In the present study, the NPV was calculated as 80%, which is the probability that individuals who score below the optimal clinical cut-off score of 64 on the IUS, truly do not have a primary anxiety disorder. An NPV of ≥80% suggests that the screening tool being utilized (i.e., IUS) is comparable to what is considered the gold standard for diagnoses (Parikh et al., 2008), such as a structured clinical interview for psychiatric disorders. Similarly, a higher PPV is recommended for clinical screening tools, as it is interpreted at the true positive rate. In this study, the PPV of the IUS was 79%, suggesting that 79% of those

individuals scoring ≥64 on the IUS did have a primary anxiety disorder. As NPV and PPV are more relevant in clinical screening, the IUS demonstrated excellent anxiety disorder screening abilities when a cut-off score of ≥64 is utilized to detect the presence of a primary anxiety disorder during the perinatal period.

2.5.1 Limitations

Although the present study was successful at revealing the use of the IUS as a screening tool for anxiety disorders during the perinatal period, there are some limitations to consider. Despite the psychometric properties of the IUS being established in non-perinatal populations, there is not an accepted clinical cut-off for anxiety disorders in those populations. Although previous research has revealed the association between perinatal anxiety and intolerance of uncertainty, which is consistent with the non-perinatal intolerance of uncertainty research, we are unable to compare whether perinatal intolerance of uncertainty levels are comparable to non-perinatal levels. The lack of a comparison group, specifically non-perinatal participants with and without anxiety disorders, is therefore a limitation of the present study. Positive and negative predictive values are highly dependent on the prevalence of a condition in the tested sample. Specifically, as the prevalence of the condition (e.g., anxiety disorder) increases, so does the positive predictive value, while the negative predictive value decreases. Although the included sample consisted of perinatal women across various settings (e.g., clinical settings, community), some participants were recruited from mental healthcare clinics and therefore the prevalence of anxiety disorders may have already been greater, which may have impacted the positive and negative predictive values. Replication studies in the future could recruit participants solely from the community, and not mental healthcare settings. Generalizability in relation to sociodemographic variables is limited, as the majority of the sample was primarily Caucasian

and highly educated. With respect to the anxiety disorder sample, the majority of participants within this group had GAD as their primary anxiety disorder. Although this is consistent with the current literature in which GAD is considered the most prevalent perinatal anxiety disorder (Fawcett et al., 2019), we were unable to determine if there are any differences in intolerance of uncertainty between anxiety disorders. Given that intolerance of uncertainty is considered a key trait across all anxiety disorders, however, we would hypothesize that future studies separating anxiety disorders during the perinatal period would yield similar results.

2.6 Conclusion

The present study was the first to investigate the psychometric properties of the IUS for use in a perinatal population. The findings demonstrate that the IUS represents a clinically meaningful screening tool to be used in perinatal populations to aid in the early and accurate detection of anxiety disorders. Higher scores on the IUS significantly predicted the presence of a primary anxiety disorder and established an optimal clinical cut-off score of ≥64. Pregnant and postpartum women who often go undiagnosed and, in turn, untreated for anxiety disorders face both short- and long-term consequences for themselves and their children. Screening measures can significantly improve symptom detection and reduce, or even prevent, these unwanted negative outcomes. Routine administration of the IUS across maternity and perinatal care settings (e.g., midwifery clinics, obstetrics and gynecology) can serve as a valuable screening tool to improve early detection of anxiety symptoms during pregnancy and the postpartum. Although the IUS consists of 27 items, the item statements are relatively concise and relatively brief to administer so as not to over burden the patient. Given the importance of intolerance of uncertainty in anxiety disorders and in predicting treatment response, the IUS is an easily

administered self-report questionnaire which may provide useful information for clinicians in early and accurate symptom detection and diagnoses.

2.7 Declarations

Acknowledgements

We would like to thank all the pregnant and postpartum women who participated in this study.

Authors' contributions

MF, BNF, and SMG were involved in writing the original study protocol. MF was involved in data collection and data analysis. BNF and SMG provided assistance and guidance in the interpretation of the study data. MF wrote the first draft of the manuscript, which was subsequently revised by BNF and SMG. All authors participated in the final approval of the manuscript.

Funding

No external funding was provided for this research. This study was funded in-kind by the Women's Health Concerns Clinic.

Availability of Data and Materials

The dataset for the current study is available from the corresponding author upon reasonable request.

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Hamilton Integrated Research Ethics Board (protocol #7568). All participants provided written informed consent.

Competing interests

The authors declare that they have no competing interests.

References

Andersson, L., Sundström-Poromaa, I., Wulff, M., Aström, M., & Bixo, M. (2004). Neonatal outcome following maternal antenatal depression and anxiety: A population-based study. *American Journal of Epidemiology, 159*(9)*,* 872-881. https://doi.org/10.1093/aje/kwh122

Anniverno, R., Bramante, A., Menacci, C., & Durbano, F. (2013). Anxiety disorders in pregnancy and the postpartum period. In F. Durbano (Ed.), *New Insights into Anxiety Disorders.* InTech. https://doi.org/10.5772/52786

Baxter, A.J., Vos, T., Scott, K.M., Ferrari, A.J., & Whiteford, H.A. (2014). The global burden of anxiety disorders in 2010. *Psychological Medicine, 44*(11)*,* 2363-2374. https://doi.org/10.1017/S0033291713003243

Bayrampour, H., Heaman, M., Duncan, K.A., & Tough, S. (2012). Advanced maternal age and risk perception: A qualitative study. *BMC Pregnancy and Childbirth, 12,* 100. https://doi.org/10.1186/1471-2393-12-100

Bernstein, G.A., Layne, A.E., Egan, E.A., & Nelson, L.P. (2005). Maternal phobic anxiety and child anxiety. *Journal of Anxiety Disorders, 19*(6), 658-672. https://doi.org/10.1016/j.janxdis.2004.09.001

Biaggi, A., Conroy, S., Pawlby, S., & Pariante, C.M. (2016). Identifying the women at risk of antenatal anxiety and depression: A systematic review. *Journal of Affective Disorders, 191,* 62-77. https://doi.org/10.1016/j.jad.2015.11.014

Blackmore, E. R., Gustafsson, H., Gilchrist, M., Wyman, C., & O'Connor, T. G. (2016). Pregnancy-related anxiety: Evidence of distinct clinical significance from a prospective longitudinal study. *Journal of Affective Disorders, 197,* 251–258. https://doi.org/10.1016/j.jad.2016.03.008

Bomyea, J., Ramsawh, H., Ball, T.M., Taylor, C.T., Paulus, M.P., Lang, A.J., & Stein, M.B. (2015). Intolerance of uncertainty as a mediator of reduction in worry in a cognitive behavioral treatment program for generalized anxiety disorder. *Journal of Anxiety Disorders, 33*, 90-94. https://doi.org/10.1016/j.janxdis.2015.05.004

Boswell, J.F., Thompson-Hollands, J., Farchione, T.J., & Barlow, D.H. (2013). Intolerance of uncertainty: A common factor in the treatment of emotional disorders. *Journal of Clinical Psychology, 69*(6), 630-645. https://doi.org/10.1002/jclp.21965

Britton, J. (2008). Maternal anxiety: Course and antecedents during the early postpartum period. *Depression and Anxiety, 25*(9), 793-800. https://doi.org/10.1002/da.20325

Buhr, K., & Dugas, M.J. (2002). The intolerance of uncertainty scale: Psychometric properties of the English version. *Behaviour Research and Therapy, 40*(8)*,* 931-945. https://doi.org/10.1016/s0005-7967(01)00092-4

Buhr, K., & Dugas, M.J. (2009). The role of fear of anxiety and intolerance of uncertainty in worry: An experimental manipulation. *Behaviour Research and Therapy, 47*(3), 215-223. https://doi.org/10.1016/j.brat.2008.12.004

Capron, L.E., Glover, V., Pearson, R.M., Evans, J., O'Connor, T.G., Stein, A., Murphy, S.E., & Ramchandani, P.G. (2015). Associations of maternal and paternal antenatal mood with offspring anxiety disorder at age 18 years. *Journal of Affective Disorders, 187,* 20-26. https://doi.org/10.1016/j.jad.2015.08.012

Chisholm, D., Sweeny, K., Sheehan, P., Rasmussen, B., Smith, F., Cuijpers, P., & Saxena, S. (2016). Scaling-up treatment of depression and anxiety: A global return on investment analysis. *The Lancet: Psychiatry, 3*(5), 415-424. https://doi.org/10.1016/S2215-0366(16)30024-4

Conference Board of Canada. (2016, September 1). Unmet mental health care needs costing Canadian economy billions. *The Conference Board of Canada.* Retrieved from http://www.conferenceboard.ca/press/newsrelease/16-09-01/unmet_mental_health_care_needs_costing_canadian_economy_billions.aspx?&utm_source=Home&utm_medium=Banner&utm_campaign=Slide1

Counsell, A., Furtado, M., Iorio, C., Anand, L., Canzonieri, A., Fine, A., Fotinos, K., Epstein, I., & Katzman, M.A. (2017). Intolerance of uncertainty, social anxiety, and generalized anxiety: Differences by diagnosis and symptoms. *Psychiatry Research, 252,* 63-69. https:doi.org/10.1016/j.psychres.2017.02.046

Cox, J.L., Holden, J.M., & Sagovsky, R. (1987). Detection of postnatal depression: development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry, 150,* 782-786. https://doi.org/10.1192/bjp.150.6.782

Dar, K.A., Iqbal, N., & Mushtaq, A. (2017). Intolerance of uncertainty, depression, and anxiety: Examining the indirect and moderating effects of worry. *Asian Journal of Psychiatry, 29*, 129-133. https://doi.org/10.1016/j.ajp.2017.04.017

Davis, E.P., & Sandman, C.A. (2010). The timing of prenatal exposure to maternal cortisol and psychosocial stress is associated with human infant cognitive development. *Child Development, 81*(1), 131-148. https:doi.org/10.1111/j.1467-8624.2009.01385.x

Davis, E.P., & Sandman, C.A. (2012). Prenatal psychobiological predictors of anxiety risk in preadolescent children. *Psychoneuroendocrinology, 37,* 1224-1233. https:doi.org/10.1016/j.psyneuen.2011.12.016

Dennis, C.L., Falah-Hassani, K., & Shiri, R. (2017). Prevalence of antenatal and postnatal

anxiety: Systematic review and meta-analysis. *The British Journal of Psychiatry, 210*(5)*,* 315-323. https://doi.org/10.1192/bjp.bp.116.187179

Dikmen-Yildiz, P., Ayers, S., & Phillips, L. (2017). Depression, anxiety, PTSD and comorbidity in perinatal women in Turkey: A longitudinal population-based study. *Midwifery, 55*, 29-37. https://doi.org/10.1016/j.midw.2017.09.001

Dugas, M.J., Gosselin, P., & Ladouceur, R. (2001). Intolerance of uncertainty and worry: Investigating specificity in a nonclinical sample. *Cognitive Therapy and Research, 25*(5), 551-558. https://doi.org/10.1023/A:1005553414688

Dugas, M.J., Buhr, K., & Ladouceur, R. (2004). The role of intolerance of uncertainly in etiology and maintenance. In R.G. Heimberg, C.L. Turk, & D.S. Mennin (Eds.), *Generalized anxiety disorder: Advances in research and practice* (pp. 77-108). Guilford Press.

Fairbrother, N., Corbyn, B., Thordarson, S.D., Ma, A., & Surm, D. (2019). Screening for perinatal anxiety disorders: Room to grow. *Journal of Affective Disorders, 250,* 363-370. https://doi.org/10.1016/j.jad.2019.03.052

Faisal-Cury, A., Menezes, P., Araya, R., & Zugaib, M. (2009). Common mental disorders during pregnancy: prevalence and associated factors among low-income women in São Paulo, Brazil. *Archives of Women's Mental Health, 12*(5), 335. https://doi.org/10.1007/s00737-009-0081-6

Fawcett, E.J., Fairbrother, N., Cox, M.L., White, I.R., & Fawcett, J.M. (2019). The prevalence of anxiety disorders during pregnancy and the postpartum period: A multivariate Bayesian meta-analysis. *Journal of Clinical Psychiatry, 80*(4), 18r12527. https://doi.org/10.4088/JCP.18r12525

Field, T., Diego, M., Hernandez-Reif, M., Figueiredo, B., Deeds, O., Ascencio, A., Schanberg,

S., & Kuhn, C. (2010). Comorbid depression and anxiety effects on pregnancy and neonatal outcome. *Infant Behavior and Development, 33*(1), 23-29. https://doi.org/10.1016/j.infbeh.2009.10.004

Freeston, M.G., Rhéaume, J., Letarte, H., Dugas, M.J., & Ladouceur, R. (1994). Why do people worry? *Personality and Individual Differences, 17*(6), 791-802. https://doi.org/10.1016/0191-8869(94)90048-5

Fresco, D. M., Mennin, D. S., Heimberg, R. G., & Turk, C. L. (2003). Using the Penn State Worry Questionnaire to identify individuals with generalized anxiety disorder: A receiver operating characteristic analysis. *Journal of Behavior Therapy and Experimental Psychiatry, 34*(3-4), 283–291. https://doi.org/10.1016/j.jbtep.2003.09.001

Furtado, M., Van Lieshout, R.J., Van Ameringen, M., Green, S.M., & Frey, B.N. (2019). Biological and psychosocial predictors of postpartum anxiety exacerbation: A longitudinal study. *Journal of Affective Disorders, 250,* 218-225. https://doi.org/10.1016/j.jad.2019.02.064

Goodman, J.H., Watson, G.R., & Stubbs, B. (2016). Anxiety disorders in postpartum women: A systematic review and meta-analysis. *Journal of Affective Disorders, 203,* 292-331. https://doi.org/10.1016/j.jad.2016.05.033

Gosselin, P., Ladouceur, R., & Pelletier, O. (2005). Evaluation of an individual's attitude toward daily life problems: The negative problem orientation questionnaire. *Journal de Thérapie Comportementale et Cognitive, 15*(4), 142-153. https://doi.org/10.1016/S1155-1704(05)81235-2

Gratz, K.L., & Roemer, L. (2004). Multidimensional assessment of emotion regulation and

dysregulation: Development, factor structure, and initial validation of the difficulties in emotion regulation scale. *Journal of Psychopathology and Behavioral Assessment, 26*, 41-54. https://doi.org/10.1023.B:JOBA.0000007455.08539.94

Grigoriadis, S., Graves, L., Peer, M., Mamisashvili, L., Tomlinson, G., Vigod, S.N., Dennis, C.L., Steiner, M., Brown, C., Cheung, A., Dawson, H., Rector, N.A., Guenette, M., & Richter, M. (2018). Maternal anxiety during pregnancy and the association with adverse perinatal outcomes: Systematic review and meta-analysis. *Journal of Clinical Psychiatry, 79*(5), 17r12011. https://doi.org/10.4088/JCP.17r12011

Grös, D.F., Antony, M.M., Simms, L.J., & McCabe, R.E. (2007). Psychometric properties of the State-Trait Inventory for Cognitive and Somatic Anxiety (STICSA): Comparison to the State-Trait Anxiety Inventory (STAI). *Psychological Assessment, 19*(4), 369-381. https://doi.org/10.1037/1040-3590.19.4.369

Hallion, L.S., Steinman, S.A., Tolin, D.F., & Diefenbach, G.T. (2018). Psychometric properties of the Difficulties in Emotion Regulation Scale (DERS) and its short form in adults with emotional disorders. *Frontiers in Psychology, 9*, 539. https://doi.org/10.3389/fpsycg.2018.00539

Harris, P.A., Taylor, R., Thielke, R., Payne, J., Gonzalez, N., & Conde, J.G. (2009). Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of Biomedical Informatics, 42*(2), 377-381. https://doi.org/10.1016/j.jbi.2008.08.010.

Hirschfeld, R.M.A. (2001). The comorbidity of major depression and anxiety disorders: Recognition and management in primary care. *Primary Care Companion Journal of Clinical Psychiatry, 3(6),* 244-254. https://doi.org/10.4088/pcc.v03n0609

Hosmer, D.W., & Lemeshow, S. (2000). *Applied Logistic Regression (2nd Ed.).* John Wiley and Sons.

Huizink, A.C., Robles De Medina, P.G., Mulderm E.J.H., Visser, G.H.A., & Buitelaar, J.K. (2002). Psychological measures of prenatal stress as predictors of infant temperament. *Journal of American Academy of Child & Adolescent Psychiatry, 41*(9)*,* 1078-1085. https://doi.org/10.1097/00004583-200209000-00008

IBM Corp. (2015). *IBM Statistics, Version 23.0.* Armonk, NY: IBM Corp.

Kashdan, T.B., Zvolensky, M.J., & McLeish, A.C. (2008). Anxiety sensitivity and affect regulatory strategies: Individual and interactive risk factors for anxiety-related symptoms. *Journal of Anxiety Disorders, 22*(3), 429–440. https://doi.org/10.1016/j.janxdis.2007.03.011

Kramer, M.S., Lydon, J., Séguin, L., Goulet, L., Kahn, S.R., McNamara, H., Genest, J., Dassa, C., Chen, M.F., Sharma, S., Meaney, M.J., Thomson, S., Van Uum, S., Koren, G., Dahhou, M., Lamoureaux, J., & Platt, R.W. (2009). Stress pathways to spontaneous preterm birth: The role of stressors, psychological distress, and stress hormones. *American Journal of Epidemiology, 169*(11)*,* 1319-1326. https://doi.org/10.1093/aje/kwp061

Levis, B., Negeri, Z., Sun, Y., Benedetti, A., Thombs, B.D., & DEPRESsion Screening Data (DEPRESSD) EPDS Group. (2020). Accuracy of the Edinburgh Postnatal Depression Scale (EPDS) for screening to detect major depression among pregnant and postpartum women: Systematic review and meta-analysis of individual participant data. *The BMJ, 371,* m4022. https://doi.org/10.1136/bmj.m4022

Lin, B., Kaliush, P.R., Conradt, E., Terrell, S., Neff, D., Allen, A.K., Smid, M.C., Monk, C., &

Crowell, S.E. (2019). Intergenerational transmission of emotion dysregulation: Part I. Psychopathology, self-injury, and parasympathetic responsivity among pregnant women. *Development and Psychopathology, 31*(3), 817-831. https://doi.org/10.1017/S0954579419000336

Martini, J., Petzoldt, J., Einsle, F., Beesdo-Baum, K., Höfler, M., & Wittchen, H.U. (2015). Risk factors and course patterns of anxiety and depressive disorders during pregnancy and after delivery: A prospective-longitudinal study. *Journal of Affective Disorders, 175,* 385-395. https://doi.org/10.1016/j.jad.2015.01.012

Matthey, S., Henshaw, C., Elliott, S., & Barnett, B. (2006). Variability in use of cut-off scores and formats on the Edinburgh Postnatal Depression Scale: Implications for clinical research practice. *Archives of Women's Mental Health, 9*(6), 309-315. https://doi.org/10.1007/s00737-006-0152-x

Matthey, S., Fisher, J., & Rowe, H. (2013). Using the Edinburgh Postnatal Depression Scale to screen for anxiety disorders: Conceptual and methodological considerations. *Journal of Affective Disorders, 146*(2), 224-230. https://doi.org/10.1016/j.jad.2012.09.009

McEvoy, P.M., & Mahoney, A.J. (2011). Achieving certainty about the structure of intolerance of uncertainty in a treatment-seeking sample with anxiety and depression. *Journal of Anxiety Disorders, 25*(1)*,* 112-122. https://doi.org/10.1016/j.janxdis.2010.08.010

Mennin, D.S., Heimberg, R.G., Turk, C.L., & Fresco, D.M. (2005). Preliminary evidence for an emotion regulation deficit model of generalized anxiety disorder. *Behaviour Research and Therapy, 43*(10), 1281–1310. https://doi.org/10.1016/j.brat.2004,08.008

Mennin, D.S., Holaway, R.M., Fresco, D.M., Moore, M.T., & Heimberg, R.G. (2007).

Delineating components of emotion and its dysregulation in anxiety and mood psychopathology. *Behavior Therapy, 38*(3), 284-302. https://doi.org/10.1016/j.beth.2006.09.001

Meyer, T. J., Miller, M. L., Metzger, R. L., & Borkovec, T. D. (1990). Development and validation of the Penn State Worry Questionnaire. *Behavior Research and Therapy, 28*(6)*,* 487–495. https://doi.org/10.1016/0005-7967(90)90135-6

Orr, S.T., Reiter, J.P., Blazer, D.G., & James, S.A. (2007) Maternal prenatal pregnancy-related anxiety and spontaneous preterm birth in Baltimore, Maryland. *Psychosomatic Medicine, 69*(6)*,* 566-570. https://doi.org/10.1097/PSY.0b013e3180cac25d

Ouellet, C., Langlois, F., Provencher, M.D., & Gosselin, P. (2019). Intolerance of uncertainty and difficulties in emotion regulation: Proposal for an integrative model of generalized anxiety disorder. *European Review of Applied Psychology, 69*(1), 9-18. https://doi.org/10.1016/j.erap.2019.01.001

Parikh, R., Mathai, A., Parikh, S., Sekhar, G.C., & Thomas, R. (2008). Understanding and using sensitivity, specificity and predictive values. *Indian Journal of Ophthalmology, 56*(1), 45-50. https://doi.org/10.4103/0301-4738.37595

Ree, M.J., French, D., MacLeod, C., & Locke, V. (2008). Distinguishing cognitive and somatic dimensions of state and trait anxiety: Development and validation of the State-Trait Inventory for Cognitive and Somatic Anxiety (STICSA). *Behavioural and Cognitive Psychotherapy, 36*(3), 313-332. https://doi.org/10.1017/S1352465808004232

Remes, O., Brayne, C., van der Linde, R., & Lafortune, L. (2016). A systematic review of reviews on the prevalence of anxiety disorders in adult populations. *Brain and Behavior, 6*(7), e00497. https://doi.org/10.1002/brb3.497

Rubertsson, C., Hellstrom, J., Cross, M., & Sydsjo, G. (2014). Anxiety in early pregnancy: Prevalence and contributing factors. *Archives of Women's Mental Health, 17*(3), 221-228. https://doi.org/10.1007/s00737-013-0409-0

Saulnier, K.G., Allan, N.P., Raines, A.M., & Schmidt, N.B. (2019). Depression and intolerance of uncertainty: Relations between uncertainty subfactors and depression dimensions. *Psychiatry: Interpersonal and Biological Processes, 82*(1), 72-79. https://doi.org/10.1080/00332747.2018.1560583.

Shorey, S., Chee, C. Y. I., Ng, E. D., Chan, Y. H., Tam, W. W. S., & Chong, Y. S. (2018). Prevalence and incidence of postpartum depression among healthy mothers: A systematic review and meta-analysis. *Journal of Psychiatric Research, 104,* 235-248. https://doi.org/10.1016/j.jpsychires.2018.08.001

Simpson, W., Glazer, M., Michalski, N., Steiner, M., & Frey, B.N. (2014). Comparative efficacy of the Generalized Anxiety Disorder 7-Item Scale and the Edinburgh Postnatal Depression Scale as screening tools for generalized anxiety disorder in pregnancy and the postpartum period. *Canadian Journal of Psychiatry, 59*(8), 434-440. https://doi.org/10.1177/0706743705900806

Smith, M.V., Shao, L., Howell, H., Wang, H., Poschman, K., & Yonkers, K.A. (2009). Success of mental health referral among pregnant and postpartum women with psychiatric distress. *General Hospital Psychiatry, 31*(2), 155-162. https://doi.org/10.1016/j.genhosppsych.2008.10.002

Somerville, S., Dedman, K., Hagan, R., Oxnam, E., Wettinger, M., Byrne, S., Coo, S., Doherty,

D., & Page, A.C. (2014). The Perinatal Anxiety Screening Scale: Development and preliminary validation. *Archives of Women's Mental Health, 17*(5), 443-454. https://doi.org/10.1007/s00737-014-0425-8

Spitzer, R.L., Kroenke, K., Williams, J.B., & Lowe, B. (2006). A brief measure for assessing generalized anxiety disorder: the GAD-7. *Archives of Internal Medicine, 166*(10)*,* 1092-1097. https://doi.org/10.1001/archinte.166.10.1092

Swanson, L. M., Pickett, S. M., Flynn, H., & Armitage, R. (2011). Relationships among depression, anxiety, and insomnia symptoms in perinatal women seeking mental health treatment. *Journal of Women's Health, 20*(4), 553–558. https://doi.org/10.1089/jwh.2010.2371

Tearne, J.E., Robinson, M., Jacoby, P., Allen, K.L., Cunningham, N.K., Li, J., & McLean, N.J. (2016). Older maternal age is associated with depression, anxiety, and stress symptoms in young adult female offspring. *Journal of Abnormal Psychology, 125*(1), 1-10. https://doi.org/10.1037/abn0000119

Tietz, A., Zietlow, A.L., & Reck, C. (2014). Maternal bonding in mothers with postpartum anxiety disorder: the crucial role of subclinical depressive symptoms and maternal avoidance behaviour. *Archives of Women's Mental Health. 17*(5), 433-442. https://doi.org/10.1007/s00737-014-0423-x

Trevethan, R. (2017). Sensitivity, specificity, and predictive values: Foundations, pliabilities, and pitfalls in research and practice. *Frontiers in Public Health, 5,* 307. https://doi.org/10.3389/fpubh.2017.00307

Tull, M.T., Rodman, S.A., & Roemer, L. (2008). Examining fear of bodily sensations and body

hypervigilance as predictors of emotion regulation difficulties among individuals with a recent history of uncued panic attacks. *Journal of Anxiety Disorders, 22*(4), 750–760. https://doi.org/10.1016/j.janxdis.2007.08.001

Tull, M.T., Stipelman, B.A., Salters-Pedneault, K., & Gratz, K.L. (2009). An examination of recent non-clinical panic attacks, panic disorder, anxiety sensitivity, and emotion regulation difficulties in the prediction of generalized anxiety disorder in an analogue sample. *Journal of Anxiety Disorders, 23*(2), 275-282. https://doi.org/10.1016/j.janxdis.2008.08.002

Van Dam, N. T., Grös, D. F., Earleywine, M., & Antony, M. M. (2013). Establishing a trait anxiety threshold that signals likelihood of anxiety disorders. *Anxiety, Stress & Coping*, *26*(1), 70–86. https://doi.org/10.1080/10615806.2011.631525

van Heyningen, T., Honikman, S., Tomlinson, M., Field, S., & Myer, L. (2018). Comparison of mental health screening tools for detecting antenatal depression and anxiety disorders in South African women. *PLoS ONE, 13*(4), e0193697. https://doi.org/10.1371/journal.pone.0193697

Wenzel, A., Haugen, E.N., Jackson, L.C., & Robinson, K. (2003). Prevalence of generalized anxiety at eight weeks postpartum. *Archives of Women's Mental Health, 6*(1), 43-49. https://doi.org/10.1007/s00737-002-0154-2.

Wenzel, A., Haugen, E.N., Jackson, L.C., & Brendle, J.R. (2005). Anxiety symptoms and disorders at eight weeks postpartum. *Journal of Anxiety Disorders, 19*(3), 295-311. https://doi.org/10.1016/j.janxdis.2004.04.001

Whiteford, H.A., Degenhardt, L., Rehm, J., Baxter, A.J., Ferrari, A.J., Erskine, H.E., Charlson,

F.J., Norman, R.E., Flaxman, A.D., Johns, N., Burstein, R., Murray, C.J.L., & Vos, T. (2013). Global burden of disease attributable to mental and substance use disorders: Findings from the Global Burden of Disease Study 2010. *Lancet, 382*(9904)*,* 1575-1586. https://doi.org/10.1016/S0140-6736(13)61611-6

Wright, K.D., Lebell, M.A., & Carleton, R.N. (2016). Intolerance of uncertainty, anxiety sensitivity, health anxiety, and anxiety disorder symptoms in youth. *Journal of Anxiety Disorders, 41,* 35-42. https://doi.org/10.1016/j.janxdis.2016.04.011

Yelland, J., Sutherland, G., & Brown, S.J. (2010). Postpartum anxiety, depression and social health: findings from a population-based survey of Australian women. *BMC Public Health, 10,* 771. https://doi.org/10.1186/1471-2458-10-771

Yook, K., Kim, K.H., Suh, S.Y., & Lee, K.S. (2010). Intolerance of uncertainty, worry, and rumination in major depressive disorder and generalized anxiety disorder. *Journal of Anxiety Disorders, 24*(6), 623-628. https://doi.org/10.1016/j.janxdis.2010.04.003

Zhong, J., Wang, C., Li, J., & Liu, J. (2009). Penn State Worry Questionnaire: Structure and psychometric properties of the Chinese version. *Journal of Zhejiang University Science B- Biomedicine & Biotechnology, 10*(3), 211-218. https://doi.org/10.1631/jzus.B0820189

Zhou, Y., Cao, Z., Yang, M., Xi, X., Guo, Y., Fang, M., Cheng, L., & Du, Y. (2017). Comorbid generalized anxiety disorder and its association with quality of life in patients with major depressive disorder. *Scientific Reports, 7,* 40511. https://doi.org/10.1038/srep40511

Chapter 3: Study Two

Cognitive behavioural therapy for intolerance of uncertainty: A study protocol for the prevention of postpartum anxiety

Furtado, M., Frey, B. N., Inness, B. E., McCabe, R. E., & Green, S. M. (2025). Cognitive behavioural therapy for intolerance of uncertainty: A study protocol for the prevention of postpartum anxiety. *Journal of Reproductive and Infant psychology*, 1–20. Advance online publication. https://doi.org/10.1080/02646838.2025.2495928

3.1 Abstract

Background: Mental health disorders are the most prevalent health complication experienced during pregnancy and the postpartum, with anxiety disorders being most common. Intolerance of uncertainty (IU) is a well-known feature of anxiety disorders and has recently been identified as a risk factor for the worsening of anxiety during the postpartum period. Cognitive Behavioural Therapy (CBT) is a first-line treatment for perinatal anxiety, and CBT specifically targeting IU in non-perinatal populations has demonstrated positive findings for reducing anxiety. As such, the objective of our study is to examine whether CBT targeting IU in pregnancy can reduce the risk of postpartum anxiety.

Methods: This protocol paper outlines a proof-of-concept randomized clinical trial assessing the effectiveness of a newly developed CBT for IU (CBT-IU) protocol to reduce the risk of postpartum anxiety. Pregnant individuals identified at increased risk for postpartum anxiety (defined as a baseline score of 64 or greater on the Intolerance of Uncertainty Scale) will be randomized to receive CBT-IU or care as usual (CAU) during pregnancy and will be followed through the postpartum period (6 – 12 weeks). The CBT-IU protocol is a weekly, six session treatment, which includes psychoeducation, behavioural experiments, imaginal exposure, and problem-solving to target IU.

Discussion: To our knowledge, this will be the first study to investigate the efficacy of a CBT protocol aimed at reducing the risk of developing postpartum anxiety. Establishing this protocol as a potentially preventative strategy will offer a new option to improve the mental health and well-being of mothers and their infants.

Clinical Trial Registration: Trial Number is NCT05691140

Keywords: perinatal, intolerance of uncertainty, anxiety, prevention, cognitive behavioural therapy

3.2 Introduction

The perinatal period, often defined as anytime throughout pregnancy and up to twelve months postpartum, is associated with increased vulnerability to experiencing mental health difficulties (Anderson et al., 2017; Awini et al., 2023; Giardinelli et al., 2012; O'Hara & Wisner, 2014; Ross & McLean, 2006; Stevenson et al., 2023; Wenzel et al., 2005; Womersley & Alderson, 2024; World Health Organization, 2022). Concerningly, mental health disorders are the most prevalent health complication experienced during the perinatal period (Howard & Khalifeh, 2020; Stevenson et al., 2023). Anxiety disorders, in particular, are the most diagnosed mental health disorder during this time, affecting between 15 - 25% of perinatal individuals (Dennis et al., 2017; Fawcett et al., 2019; Roddy Mitchell et al., 2023). Anxiety disorders during the perinatal period are associated with increased rates of obstetric complications, such as preeclampsia, longer and more difficult delivery, and delivering pre-term (Anniverno et al., 2013; Dowse et al., 2020; Hoyer et al., 2020; Littleton et al., 2007; Qiu et al., 2009; Sanni et al., 2022; Toscano et al., 2021; Weis et al., 2020). Individuals with anxiety during the perinatal period also experience an increased risk of substance use disorders, recurrent mental health difficulties, and suicide (Chin et al., 2022; Dennis et al., 2017; Orsolini et al., 2016; Pentecost et al., 2021). Adverse outcomes extend to the infant, in which they are more likely to experience cognitive and motor deficits, poorer attention and self regulation (Blair et al., 2011; Brand & Brennan, 2009; Britton, 2011; Hennessey et al., 2023; Huizink et al., 2002; Irwin et al., 2020; Ross et al., 2020; Schwarze et al., 2024; Weis et al., 2020), as well as heightened negative affect (Blair et al., 2011; Rogers et al., 2020; Spry et al., 2020; Vismara et al., 2020).

Among the known psychological risk factors of anxiety during the perinatal period is intolerance of uncertainty (Furtado et al., 2019). In this study, pregnant individuals were followed throughout pregnancy to six months postpartum to identify psychological risk factors of

postpartum anxiety worsening. Psychological factors assessed included intolerance of uncertainty, sleep difficulties, history of childhood trauma, as well as anxiety, depression, and obsessive-compulsive symptoms. The psychological factors identified as significantly increasing risk of postpartum anxiety, were depression and obsessive-compulsive symptoms during pregnancy, and intolerance of uncertainty. This was the first study to demonstrate the role of intolerance of uncertainty in increasing postpartum anxiety risk. Intolerance of uncertainty (IU), commonly defined as a fear of the unknown (Carleton, 2016), is considered a cardinal feature of anxiety, both as a risk factor and a symptom maintenance factor (Carleton, 2012; Counsell et al., 2017; Dugas & Robichaud, 2007; Gu et al., 2020; Morriss et al., 2023; Wilson et al., 2023). While most individuals prefer certainty and predictability, those high in IU perceive danger in everyday situations where those with low IU do not. This misinterpretation often leads to excessive safety behaviours, such as avoidance, checking, and reassurance seeking (Hebert & Dugas, 2019). For example, an individual high in IU who is tasked with making a decision might seek excessive reassurance from others, excessive researching, and procrastinate due to the fear that they will make the wrong decision and it can't be fixed. Within the perinatal context, individuals high in IU may engage in these behaviours when deciding what baby-related items (e.g., car seat, crib mattress) to purchase, with the goal of making the "right" decision. Whereas an individual low in IU will be able to make a decision quicker, because they hold more balanced beliefs that they likely will not make the wrong decision, or even if they do, it can be fixed. High IU in the perinatal period has also been shown to be associated with fear of childbirth (Flink et al., 2023; Han et al., 2022; Rondung et al., 2019), and related safety behaviours may include excessive researching and reassurance seeking (e.g., internet, health care providers). In the postpartum period, individuals high in IU may be more likely engage in safety behaviours

associated with the baby's health (e.g., excessive checking of breathing when sleeping). IU has also been shown to be a significant predictor and mediator of cognitive behavioural therapy (CBT) treatment response, specifically related to reductions in worry and anxiety (Bomyea et al., 2015; Katz et al., 2017; Marcotte-Beaumier et al., 2021; Miller & McGuire, 2023). CBT is a first-line treatment for both non-perinatal anxiety disorders (Bandelow et al., 2017; Katzman et al., 2014) and anxiety disorders during the perinatal period (National Institute for Health and Care Excellence, 2020; Shea et al., 2024; Vigod et al., 2025), and CBT programs targeting IU have revealed promising findings in *non-perinatal* populations (Hebert & Dugas, 2019; Dugas & Ladouceur, 2000; Robichaud, 2013; van der Heiden et al., 2012; Wilson et al., 2023; Zemestani et al., 2021). CBT that directly targets IU has been shown to be significantly more effective at reducing both IU and worry symptoms compared to general CBT from pre- to post-treatment in individuals with Generalized Anxiety Disorder (GAD; Wilson et al., 2023). Additionally, Zemestani and colleagues (2021) recently found that CBT targeting IU produced significantly better treatment outcomes for GAD, when compared to use of selective serotonin reuptake inhibitors post-treatment. These CBT-IU protocols primarily consist of engaging in behavioural experiments, in which individuals are able to directly test their feared IU predictions (i.e., uncertain situations lead to negative outcomes) and work toward holding more balanced beliefs about uncertainty (e.g., uncertain situations will probably turn out okay) by gathering personal evidence from the experiments (Hebert & Dugas, 2019; Dugas & Ladouceur, 2000; Robichaud, 2013; van der Heiden et al., 2012; Wilson et al., 2023; Zemestani et al., 2021). Other commonly used CBT-IU strategies include imaginal exposure, which targets cognitive avoidance related to uncertainty, as well as problem-solving strategies for working with productive worries related to uncertainty (Dugas & Ladouceur, 2000; Robichaud, 2013; van der Heiden et al., 2012).

Given the role of IU as a risk factor for postpartum anxiety worsening (Furtado et al., 2019), we developed a CBT protocol specifically designed to reduce IU during pregnancy to reduce the risk of postpartum anxiety. The primary aim of this study is to evaluate whether a brief, six session individual CBT protocol targeting IU (CBT-IU) in pregnant individuals with heightened levels of IU can reduce risk of postpartum anxiety onset, when compared to care as usual (CAU). We hypothesize that perinatal individuals with clinically significant IU during pregnancy will exhibit both reductions in IU, as well as a decreased risk of developing an anxiety disorder during the postpartum, when compared to CAU. To our knowledge, this will be the first study to investigate the efficacy of a CBT protocol specifically aimed to reduce the risk of anxiety disorders during the postpartum.

3.3 Methods

3.3.1 Inclusion/Exclusion Criteria

The study sample will include participants who are/have: (1) pregnant individuals (between 14 to 32 weeks pregnant); (2) 18 years or older; (3) a baseline score of 64 or greater on the IUS (Furtado et al., 2021); (4) no current psychotropic medication use or, if taking medication, no change in dose or type for a minimum of six weeks prior to baseline; (5) no concurrent psychological treatment; and (6) fluent in English and able to consent for treatment. With respect to weeks gestation, given that the first trimester of pregnancy is associated with increased medical risk, this may be associated with expected levels of increased anxiety and uncertainty. Therefore, participants will only be recruited beginning in their second trimester of pregnancy (≥14 weeks). Additionally, eligible participants cannot be more than 32 weeks pregnant at baseline, to allow for completion of the CBT-IU treatment protocol prior to delivery (if randomized to CBT-IU).

Participants will be excluded if they are: (1) currently diagnosed with a DSM-5 anxiety disorder at baseline (as assessed by the MINI); (2) actively suicidal at baseline, in which they will be provided with appropriate resources; or (3) diagnosed with a psychotic disorder, or current substance or alcohol use disorder.

3.3.2 Sample Size

As this is a proof-of-concept randomized controlled trial, we will employ a commonly used method in which a minimum of 30 participants are required to estimate a parameter (Whitehead et al., 2016). As the present study includes an experimental (CBT-IU) and control (care as usual) arm, a minimum of 15 participants will be randomized to each arm. To account for a 20% attrition rate, 38 participants will be recruited overall.

3.3.3 Study Design

This study is an investigator-initiated, single center, randomized controlled trial, taking place at the Women's Health Concerns Clinic (WHCC), St. Joseph's Healthcare Hamilton, Canada. Participants will be recruited through referrals and postings displayed throughout the WHCC and outpatient clinics at St. Joseph's Healthcare Hamilton. Recruitment advertisements will also be posted throughout the community, predominantly in obstetric, family physician, and midwifery clinics, as well as in other Ontario community areas and online. As all study visits are completed virtually, recruitment will take place across Ontario, Canada. This study has received approval by the Hamilton Integrated Research Ethics Board (HiREB #13902), in accordance with the Declaration of Helsinki.

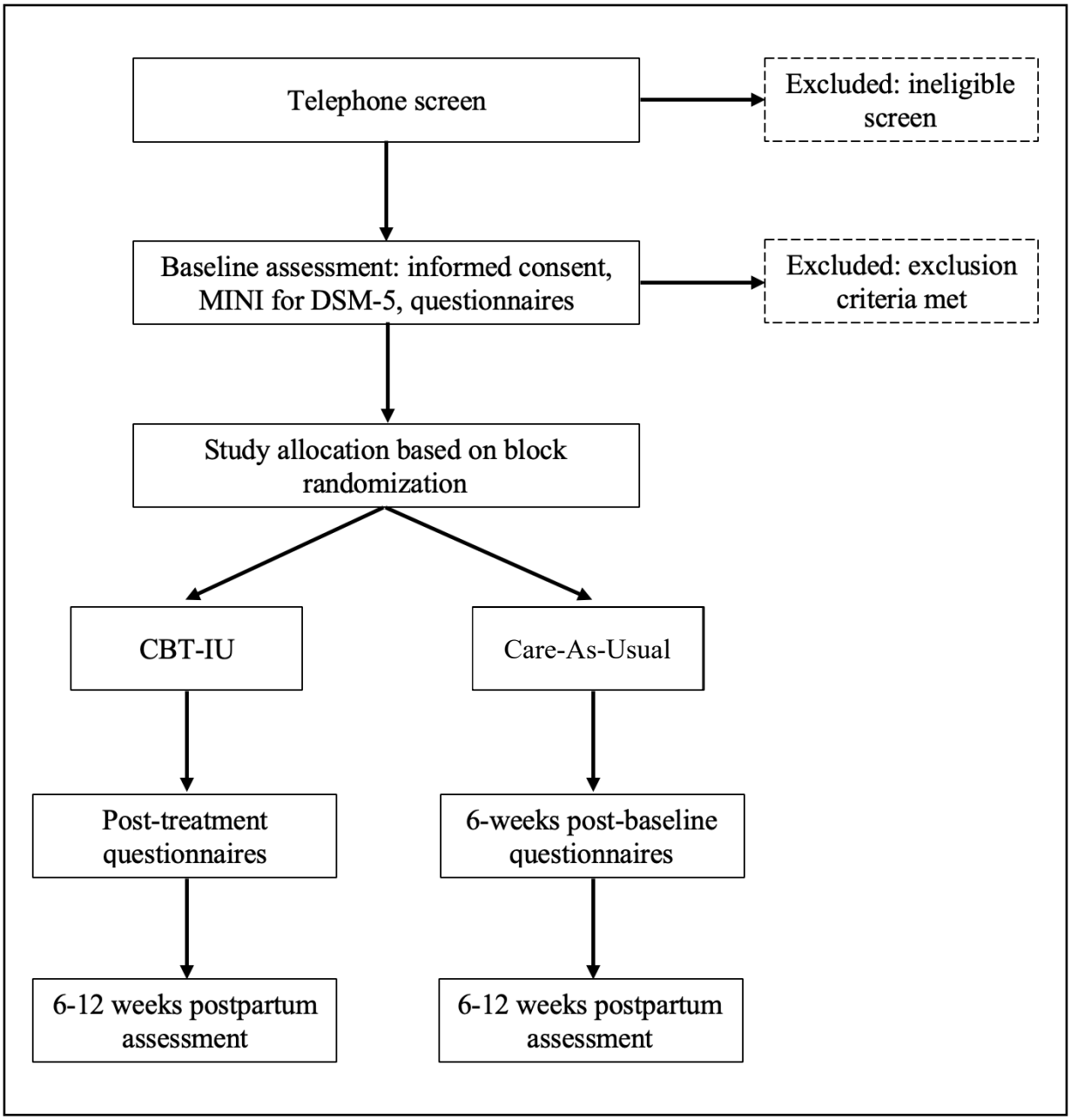
Individuals who are interested in participating will be contacted via telephone to complete an initial eligibility screening, and if eligible, will be scheduled for a baseline assessment. Prior to beginning the baseline assessment, participants review the informed consent

form with the investigator conducting the assessment, providing the opportunity for a question-and-answer period. A fully signed copy of the informed consent form, that is password protected, is then shared via email with the participant. After the consent process, participants begin the baseline assessment in which any psychiatric diagnoses are determined, through use of the Mini International Neuropsychiatric Interview for DSM-5 version 7.0.2 (MINI). During the baseline assessment, participants also provide a perinatal and medical history (e.g., medication and psychotherapy history, planned method of delivery), and complete a symptom assessment battery of questionnaires (see Study Measures), including the IUS to determine eligibility. Following confirmation of eligibility, participants will be randomly assigned by the first author (MF) to the experimental CBT-IU or CAU control condition. The block randomization method will be used to result in equal sample sizes between the CBT-IU and CAU groups. Prior to the start of the first participant being enrolled in the study, a block randomization list was created. Once a participant is deemed eligible, the first author accesses the block randomization list and assigns the participant to the next available group (i.e., CBT-IU or no intervention group). Ineligible participants will be provided with a list of additional resources, when applicable (i.e., if a participant is diagnosed with a current untreated anxiety disorder). A battery of symptom assessment questionnaires will also be administered within two weeks following treatment/control (e.g., 6 – 8 weeks post-baseline), and again between 6 – 12 weeks postpartum. Please see **Figure 1** for a flowchart outlining the study procedures.

If participants who are randomized to CAU exhibit clinically significant symptoms of an anxiety and/or mood disorder at either the post-control or postpartum assessment, they will be offered clinical care (e.g., group CBT), as needed. Similarly, for those randomized to CBT-IU, if clinically significant symptoms are present at the postpartum time point, these same resources

will be offered. To reduce attrition, all participants will be compensated following each assessment time point with a $20 e-gift card.

Figure 1. Flowchart of study procedures.



Note: All study visits following the telephone screenings are completed via the Zoom virtual platform.

3.3.4 Virtual Study Visits

To ensure accessibility for all participants who may be unable to attend in-person visits and given that we will recruit participants from an extended geographic area, all study visits will be completed virtually via Zoom. The Zoom Video Communications platform provides videotelephone and online chat services through a cloud-based peer-to-peer software platform, used for teleconferencing, telecommuting, distance education, and social relations. Zoom is compliant with the Personal Information Protection and Electronic Documents Act and the Personal Health Information Protection Act. A section detailing virtual visits and the guidelines for participation (e.g., ensuring participants are in a private space, not using recording devices) is included in the informed consent form.

3.3.5 Study Measures

The assessment battery will include various interviewer-rated and self-report measures of intolerance of uncertainty, anxiety, worry, and mood symptoms, as well as measures assessing emotion regulation, traumatic stress, and treatment satisfaction. See **Table 1** for a list of study measures and their associated timing.

Table 1. Schedule of study measurements.

Procedures and Measures	**Baseline**	**Post-treatment**	**Postpartum**
Enrolment			
Informed consent	X		
Randomization	X		

Structured Interview			
MINI for DSM-5	X		
Primary Outcomes			
Postpartum Anxiety Prevention[a]			X
Intolerance of Uncertainty Scale	X	X	X
Secondary Outcomes			
Hamilton Anxiety Rating Scale	X	X	X
Generalized Anxiety Disorder 7-item Scale	X	X	X
Edinburgh Postnatal Depression Scale	X	X	X
Penn State Worry Questionnaire	X	X	X
Difficulties in Emotion Regulation Scale	X	X	X
Posttraumatic Stress Disorder Checklist for DSM-5[b]	X	X	X
Client Satisfaction Questionnaire[c]		X	
Other Factors			
Demographics and Medical History	X		
Obstetric Information	X	X	X

[a]*Postpartum anxiety prevention is assessed through use of the anxiety and related disorders MINI modules.*

[b]*Only completed by participants endorsing a criterion A trauma at baseline or postpartum (related to traumatic childbirth).*

[c]*Only completed by participants in the CBT-IU group.*

3.3.5.1 Primary Outcomes

Postpartum Anxiety Prevention

To assess our primary outcome of postpartum anxiety prevention, the anxiety and related disorders MINI modules will be readministered at the postpartum time point (between 6 – 12 weeks postpartum). The MINI is a semi-structured diagnostic interview of major psychiatric disorders in the DSM-5 and has demonstrated similar validity and reliability properties to other commonly used diagnostic interviews (e.g., SCID). At the postpartum timepoint, the MINI diagnostic modules for anxiety disorders (e.g., Generalized Anxiety Disorder, Social Anxiety Disorder, Panic Disorder, Agoraphobia, and Specific Phobia), as well as other anxiety-related disorders (e.g., Obsessive-Compulsive Disorder, Posttraumatic Stress Disorder) will be administered. Prevention of postpartum anxiety will be defined for those participants who do not meet a *provisional* diagnosis of any of the aforementioned anxiety or related disorders at the postpartum time point. Given the length of symptom duration necessary to meet diagnostic criteria for certain DSM-5 anxiety and related disorders (e.g., minimum of six months for Generalized Anxiety Disorder), and as participants are only followed until 6 – 12 weeks postpartum, we will use *provisional* diagnostic criteria. Specifically, participants must fulfill all other DSM-5 criteria aside from timeline, particularly whether symptoms experienced are significantly distressing and/or impairing functioning, to meet for a provisional postpartum diagnosis.

Intolerance of Uncertainty Scale

The Intolerance of Uncertainty Scale (IUS) is a 27-item self-administered questionnaire assessing intolerance of uncertainty (Buhr & Dugas, 2002), which is a predominant characteristic of anxiety disorders. Items on the IUS are rated on a 5-point Likert type scale ranging from 1

(not at all characteristic of me) to 5 (entirely characteristic of me), with higher total scores indicating greater difficulties with tolerating uncertainty. The IUS has demonstrated excellent internal consistency ($\alpha = 0.91 – 0.95$) and good test-retest reliability ($r = 0.78$) in non-perinatal populations (Buhr & Dugas, 2002). Within a perinatal population, an optimal clinical cut-off score of 64 or greater has been established for detecting probably anxiety disorder diagnoses with a sensitivity of 89% and specificity of 65% (Furtado et al., 2021). The IUS has also demonstrated excellent internal consistency ($\alpha = 0.95$), test-retest reliability ($r = 0.91$), and very good positive (79%) and negative (80%) predictive values in a perinatal population (Furtado et al., 2021).

3.3.5.2 Secondary Outcomes

Hamilton Anxiety Rating Scale

The Hamilton Anxiety Rating Scale (HAM-A) is a 14-item interviewer administered scale (Hamilton, 1959) assessing overall anxiety symptom severity across two subscales: psychic anxiety (i.e., psychological distress, fears) and somatic anxiety (i.e., physical symptoms related to anxiety). Items are assessed on individualized 4-point Likert scales, with higher scores indicating greater anxiety severity. The HAM-A is considered a gold-standard measure of anxiety symptoms worldwide, and will be used in this study as the interviewer-rated measure to assess anxiety symptom severity. The HAM-A has demonstrated excellent internal consistency ($\alpha = 0.82 – 0.92$) and test-retest reliability ($r = 0.89$) in anxiety and depression populations (Hallit et al., 2020; Maier et al., 1988; Shear et al., 2001).

Generalized Anxiety Disorder 7-Item Scale

The Generalized Anxiety Disorder 7-Item Scale (GAD-7) is a 7-item self-report questionnaire assessing anxiety symptom severity over the previous two-week period (Spitzer et

al., 2006). Items are measured on a 4-point Likert scale ranging from 0 (not at all) to 3 (nearly every day). The GAD-7 will be used in this study as the self-report measure assessing participant's anxiety symptom severity at each time point. The GAD-7 has demonstrated excellent internal consistency (α = 0.88 – 0.93; Johnson et al., 2019; Löwe et al., 2008; Spitzer et al., 2006; Villarreal-Zegarra, 2024) and test-retest reliability (ICC= 0.83; Spitzer et al., 2006, r = 0.87; Bischoff et al., 2020). When using a cut off score of 10 or greater, the GAD-7 has demonstrated good sensitivity (89%) and specificity (82%) in detecting a diagnosis of GAD (Spitzer et al., 2006. The GAD-7 has also been validated in the perinatal populations, demonstrating excellent internal consistency (α = 0.91; Vogazianos et al., 2022), and adequate sensitivity (61.3%) and specificity (72.7%) when an optimal cut of score of 13 or greater is used (Simpson et al., 2014).

Edinburgh Postnatal Depression Scale

The Edinburgh Postnatal Depression Scale (EPDS) is a 10-item self-report questionnaire assessing perinatal depression symptoms (Cox et al., 1987). Items are scored on a 4-point Likert scale (scores ranging from 0 to 3), with higher total scores indicating greater severity of depressive symptoms. Given the overlap between anxiety and depression, the EPDS will be included to identify whether there are any differences in depression symptom severity between the CBT-IU and CAU groups. The EPDS has demonstrated good internal consistency (α = 0.82 – 0.83; Bunevicius et al., 2020; Smith-Nielsen et al., 2018; Wagner Moyer et al., 2024). A cut-off score of 11 or higher has been recommended (Levis et al., 2020), in place of the more commonly used cut-off of 13 or higher (Hewitt et al., 2009), as it maximizes combined sensitivity (0.81) and specificity (0.88). The EPDS has also demonstrated good test-restest reliability (ICC=0.92; Kernot et al., 2015).

Penn State Worry Questionnaire

The Penn State Worry Questionnaire (PSWQ) is a 16-item self-report questionnaire designed to assess worry symptoms (Meyer et al., 1990). Items are measured on a 5-point Likert scale ranging from 1 (not at all typical of me) to 5 (very typical of me), with higher scores indicating increased pathological worry. The PSWQ has long been considered the gold-standard in assessing worry symptoms, and will be used in this study to assess whether the CBT-IU protocol reduces worry when compared to CAU. The PSWQ has demonstrated excellent internal consistency (α = 0.92 -0.95; Brown et al., 1992; Inness et al., 2023; Rodriguez-Biglieri & Vetere, 2011; Voegtline et al., 2021) and test-retest reliability (r = 0.82 – 0.92; Meyer et al., 1990; Rodriguez-Biglieri & Vetere, 2011) across various populations. The PSWQ has been used in numerous studies to assess pathological worry in the perinatal population (Blackmore et al., 2016; Goldfinger et al., 2020; Goodman et al., 2014; Green et al., 2020, 2021; Mourady et al., 2017). An optimal clinical cut-off score of 55 and 61 or greater was recently shown to detect probable GAD during pregnancy and the postpartum period, respectively (Inness et al., 2023).

Difficulties in Emotion Regulation Scale

The Difficulties in Emotion Regulation Scale (DERS) is a 36-item self-report questionnaire (Gratz & Roemer, 2004) assessing six dimensions of emotion regulation: non-acceptance, goals, impulse, awareness, strategies, and clarity. Items are rated on a 5-point Likert scale ranging from 1 (almost never, 0 – 10%) to 5 (almost always, 91 – 100%), with higher scores indicating more difficulties with emotion regulation. The DERS has demonstrated good internal consistency (α = 0.82 – 0.94; Barrett et al., 2023; Hallion et al., 2018; Gratz & Roemer, 2004) and test-retest reliability (r = 0.88; Gratz & Roemer, 2004) in non-perinatal and perinatal populations. An optimal cut-off score of 87 or greater has demonstrated good sensitivity (81%)

for detecting a probable anxiety, depressive, and/or trauma-related disorder (Barrett et al., 2023). Emotion dysregulation is a known transdiagnostic factor associated with the development and maintenance of anxiety disorders (Hofman et al., 2012; Sloan et al., 2017), and has recently been shown to be associated with perinatal anxiety (Agako et al., 2021). Individuals with high IU are also more likely to experience an increase in maladaptive emotion regulation strategies (Sahib et al., 2023). Given the relationship between emotion dysregulation, intolerance of uncertainty, and perinatal anxiety, we are interested in determining whether CBT-IU can improve emotion regulation.

Posttraumatic Stress Disorder Checklist for DSM-5

The Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5) is a 20-item self-report questionnaire assessing the DSM-5 symptoms of Posttraumatic Stress Disorder (PTSD; Weathers et al., 2013). The PCL-5 has been used as a self-report measure to monitor symptom change, screen individuals for PTSD, as well as to make provisional PTSD diagnoses. Items are scored on s 5-point Likert scale ranging from 0 (not at all) to 4 (extremely), with a suggested clinical cut-off score of 33 or greater. The PCL-5 has demonstrated excellent internal consistency (α = 0.94 – 0.96), test-retest reliability (r = 0.82- 0.86), as well as convergent and discriminant validity (Blevins et al., 2015; Bovin et al., 2016). The PCL-5 has also been recently validated in a postpartum population (in relation to PTSD stemming from a traumatic childbirth), in which it exhibited excellent internal consistency (α = 0.93; Hemant Arora et al., 2024). In the present study, the PCL-5 will only be administered if participants endorse a Criterion A traumatic event(s) at baseline or the postpartum timepoint (e.g., traumatic childbirth experience), and scores will be included as a covariate.

Client Satisfaction Questionnaire

The Client Satisfaction Questionnaire (CSQ) is an 8-item self-report questionnaire designed to measure client satisfaction with health services (Larsen et al., 1979). Items are scored on a 4-point Likert scale ranging from 1 to 4 (various item labels are used), with higher scores indicating higher levels of satisfaction with the service received. The CSQ has demonstrated excellent internal consistency ($\alpha = 0.92 – 0.93$). Only participants randomized to CBT-IU will complete the CSQ. Qualitative questions assessing participants satisfaction with the CBT-IU program will also be included.

3.3.5.3 Other Factors

Demographics and Medical History

Information pertaining to participant's age, gender identity, race, marital status, parity, education level, medical history, etc., will be collected.

Obstetric Information

Participants will be asked about their planned method of delivery (e.g., vaginal, caesarian section) and location of delivery (e.g., home vs. hospital) at the baseline visit, as well as the post-treatment visit (to assess if there have been any changes in the plan). At the postpartum visit, information will be collected pertaining to the participant's actual method of delivery, whether there were any birth and/or delivery complications (e.g., pre-term birth, placenta previa, NICU admission, etc.).

3.3.6 Study Arms

Care As Usual

The CAU study arm will serve as the control condition, in which participants will not be assigned to any type of study intervention. To resemble real world settings, participants in CAU

will not be excluded from the study if they initiate any type of psychological treatment during the course of the study following randomization. Any initiated treatments will be recorded at the study visits and controlled for in the analyses. If participants who are randomized to CAU experience any distressing mental health symptoms (e.g., anxiety, worry, depression) they will be asked to notify the first author so that appropriate services are offered, as needed. At the postpartum study timepoint, if participants in CAU are meeting diagnostic criteria for a provisional anxiety or related disorder, they will be offered standard services within the WHCC, such as group CBT for perinatal anxiety.

Cognitive Behavioural Therapy Targeting Intolerance of Uncertainty for Postpartum Anxiety Prevention

CBT-IU will be offered to those randomized to this study arm in an individual format. This protocol will consist of six one-hour sessions that take place weekly during pregnancy (any time after 14 weeks' gestation and beginning by 32 weeks' gestation to ensure protocol completion prior to delivery). Sessions will be delivered by one of two trained, senior level Ph.D. students in clinical psychology (MF or BEI), supervised by a licensed clinical psychologist (SMG). The content provided during each session will include psychoeducation about the nature of anxiety during the perinatal period and the intolerance of uncertainty construct, as well as evidence-based behavioural and cognitive strategies designed to target intolerance of uncertainty. Participant worksheets will be developed based upon previous CBT for IU protocols used in non-perinatal populations (Dugas et al., 2022; Hebert & Dugas, 2019; Robichaud, 2013; van der Heiden et al., 2012), as well as a CBT for perinatal anxiety protocol (primarily for perinatal anxiety psychoeducation; Green et al., 2018). The content provided in each session is detailed in **Table 2.**

Table 2. CBT-IU Session-by-Session Content.

Session 1	- Orientation to treatment - Psychoeducation on prevalence and risk factors of anxiety disorders during the perinatal period - Introduction to the role of intolerance of uncertainty - Negative and balanced beliefs about uncertainty - Manifestations of uncertainty (safety-seeking behaviours) - Introduction of CBT principles and model - Introduction to worry awareness training and worry monitoring forms
Session 2	- Check-in and review of homework - Introduction to CBT-IU model - Psychoeducation on selective attention and confirmation bias - Challenging beliefs about uncertainty - Behavioural experiments on testing feared and actual outcomes and coping
Session 3	- Check-in and review of homework - Continuation of behavioural experiments - Learning to reflect on behavioural experiment outcomes - Introduction to the association between uncertainty and perfectionism - Adapting behavioural experiments for perfectionism
Session 4	- Check-in and review of homework - Psychoeducation on cognitive avoidance - Introduction to principles of exposure

	- Rationale and guidelines for imaginal exposure as an alternative to cognitive avoidance
Session 5	- Check-in and review of homework - Role of intolerance of uncertainty in decision making - Problem orientation and uncertainty - Problem-solving training
Session 6	- Check-in and review of homework - Learning to embrace uncertainty - Review of strategies and reflecting on behavioural experiments - Identifying early warning signs for relapse prevention - Identifying long-term goals and plan for maintaining gains

3.4 Data Management and Analysis

Data collected for this study will be recorded and electronically stored and managed using Research Electronic Data Capture (REDCap). REDCap is a secure, meta-driven web-application used to build online databases, which was developed with support from the National Centre for Research Resources (NCRR) and the National Institutes of Health (NIH). REDCap follows strict regulatory compliance with standards including the Health Insurance Portability and Accountability Act (HIPAA) and the Federal Information Security Management Act (FISMA), in addition to other international standards. In this study, only the electronic consent forms will contain the participant's full names, and these consent forms will be password protected and stored separately from all other participant documents. Once obtaining informed consent, participants will be assigned with a de-identified code, and only this code will be recorded within REDCap. A list containing the participant codes and associated participant

names will be stored in a password protected document and stored separately from all other study documents to ensure participant confidentiality.

Postpartum anxiety prevention will be determined through the absence of a provisional anxiety and/or related disorder diagnosis in the postpartum. To determine whether engaging in CBT-IU decreases the risk of receiving a provisional anxiety and/or related disorder diagnosis, a logistic regression will be completed to control for covariates (e.g., history of CBT before and/or during study). A series of repeated measures analysis of variance (ANOVA) will be used to examine condition differences. A two (CBT-IU versus CAU) by two (time: baseline, post-treatment/baseline) repeated measures ANOVA will be used to examine differences in anxiety symptom severity. Repeated measures ANOVA will also be used to assess differences in secondary outcomes (e.g., depression, worry). To determine if any benefits are maintained long-term, a within-subject repeated measures ANOVA will be conducted for the CBT-IU group across three testing times (baseline, post-treatment, and 6-12 weeks postpartum). Long-term symptoms changes will also be assessed in the CAU group across the three testing time points. Non-parametric tests will be used, if necessary, and alpha levels will be set at 0.05.

3.5 Dissemination

Study results will be disseminated through open-access, peer-reviewed scientific publications, as well as at relevant national and international conferences (e.g., Canadian Psychological Association, Association of Behavioral and Cognitive Therapies). Results will be also disseminated to healthcare professionals (e.g., clinical grand rounds, workshops), relevant organizations (e.g., Canadian Perinatal Mental Health Collaborative), and in the form of media outlets (e.g., social media platforms). A lay information package summarizing study results will be constructed for any participant who expresses interest in receiving the results of the study.

Researchers on the study team (e.g., co-investigators, collaborators) who have made significant contributions to the design, implementation, and analysis of study data will be granted authorship for planned and unplanned publications.

3.6 Discussion

Establishing this CBT-IU protocol as a preventative, and potentially cost-effective strategy will directly impact the mental health and well-being of mothers and their infants, an often underserved population. While the intention of this CBT-IU protocol is to primarily prevent postpartum anxiety and reduce IU, we also anticipate reductions, and possible prevention of postpartum mood worsening (e.g., postpartum depression). To our knowledge, this study will be the first to investigate the efficacy of a psychological therapy protocol aimed at reducing the risk of developing anxiety disorders in the postpartum period. This study may also provide the basis for a larger randomized controlled trial to establish the efficacy of this CBT-IU protocol in the prevention of postpartum anxiety. If this study does demonstrate anticipated promising findings, results may not be generalizable with respect to preventing postpartum anxiety disorders as a whole. Larger trials with longitudinal timepoints (e.g., 12 months postpartum) would be required in the future to apply the anticipated findings of the present study more broadly. As consumer demand increases for alternative treatments for anxiety disorders during the perinatal period, this treatment strategy may not only be preferred by some, but this study may also have a direct cost-effective impact on healthcare service delivery, by using a manualized psychotherapy approach in which healthcare professionals can be trained on. Given the numerous negative effects associated with anxiety during the perinatal period, this protocol has the potential to decrease and potentially prevent the emotional and functional impairments

associated with anxiety disorders during the perinatal period and improve health outcomes and well-being.

3.7 Declarations

Acknowledgements

The authors would like to sincerely thank all perinatal individuals who have participated in this study to date.

Disclosure Statement

No potential conflict of interest was reported by the author(s).

Funding

This study was funded by an unrestricted educational gift from Shoppers Drug Mart (Run for Women) and in-kind by the Women's Health Concerns Clinic, St. Joseph's Healthcare Hamilton. The first author (MF) is supported by the Ontario Women's Health Scholar Award.

Availability of Data and Materials

Data sharing is not applicable to this article as no datasets were generated or analyzed for this article.

Author Contributions

MF is a co-investigator of this study and contributed to the conceptualization, methodology, project administration, writing and editing. BNF is a co-investigator and contributed to the conceptualization, methodology, writing, and editing. BEI is a co-investigator and contributed to the project administration, writing, and editing. REM is a co-investigator and contributed to the methodology, writing, and editing. SMG is the principal investigator and contributed to the conceptualization, methodology, writing, and editing. All authors contributed to the article and approved the submitted version.

Ethics Statement

This study was reviewed and approved by the Hamilton Integrated Research Ethics Board (HiREB). The participants in this study will provide their informed consent to participate before engaging in any study-related assessments.

References

Agako, A., Donegan, E., McCabe, R.E., Frey, B.N., Streiner, D., & Green, S. (2021). The role of emotion dysregulation in cognitive behavioural group therapy for perinatal anxiety: Results from a randomized controlled trial and routine clinical care. *Journal of Affective Disorders, 292*, 517-525. https://doi.org/10.1016/j.jad.2021.05.084

Anniverno, R., Bramante, A., Mencacci, C., & Federico, D. (2013). Anxiety disorders in pregnancy and the postpartum period. In D. Federico (Ed.), *New Insights into Anxiety Disorders*. InTech.

Antony, M. M., Bouchard, S., Brunet, A., Flament, M., Grigoriadis, S., Mendlowitz, S., O'Connor, K., Rabheru, K., Richter, P. M. A., Robichaud, M., & Walker, J. R. (2014). Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders. *BMC Psychiatry, 14 Suppl*(Suppl 1), S1. https://doi.org/10.1186/1471-244X-14-S1-S1

Bandelow, B., Michaelis, S., & Wedekind, D. (2017). Treatment of anxiety disorders. *Dialogues in Clinical Neuroscience, 19*(2), 93-107. https://doi.org/10.31887/DCNS.2017.19.2/bbandelow

Barrett, E.N., Frey, B.N., Streiner, D.L, Agako, A., Inness, B.E., Furtado, M., Caropreso, L., & Green, S.M. (2023). Psychometric properties of the Difficulties in Emotion Regulation Scale in a perinatal sample. *Journal of Reproductive and Infant Psychology,* 1-20. https://doi.org/10.1080/02646838.2023.2227648

Bischoff, T., Anderson, S.R., Heafner, J., & Tambling, R. (2020). Establishment of a reliable change index for the GAD-7. *Psychology, Community & Health, 8*(1), 176-187.

Blackmore, E.R., Gustafsson, H., Gilchrist, M., Wyman, C., & O'Connor, T.G. (2016).

Pregnancy-related anxiety: Evidence of distinct clinical significance from a prospective longitudinal study. *Journal of Affective Disorders, 197,* 251-258. https://doi.org/10.1016/j.jad.2016.03.008

Blair, M.M., Glynn, L.M., Sandman, C.A., & Poggi Davis, E. (2011). Prenatal maternal anxiety and early childhood temperament. *Stress, 14*(6), 644-651. https://doi.org/10.3109/10253890.2011.594121

Blevins, C.A., Weathers, F.W., Davis, M.T., Witte, T.K., & Domino, J.L. (2015). The Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5): Development and Initial Psychometric Evaluation. *Journal of Traumatic Stress, 28*(6), 489-498. https://doi.org/10.1002/jts.22059

Bomyea, J., Ramsawh, H., Ball, T.M., Taylor, C.T., Paulus, M.P., Lang, A.J., & Stein, M.B. (2015). Intolerance of uncertainty as a mediator of reductions in worry in a cognitive behavioural treatment program for generalized anxiety disorder. *Journal of Anxiety Disorders, 33,* 90-94. https://doi.org/10.1016/j.janxdis.2015.05.004

Bovin, M.J., Marx, B.P., Weathers, F.W., Gallagher, M.W., Rodriguez, P., Schnurr, P.P., & Keane, T.M. (2016). Psychometric properties of the PTSD Checklist for Diagnostic and Statistical Manual of Mental Disorders—Fifth Edition (PCL-5) in veterans. *Psychological Assessment*, *28*(11), 1379-1391. https://doi.org/10.1037/pas0000254

Brand, S.R., & Brennan, P.A. (2009). Impact of antenatal and postpartum maternal mental illness: How are the children? *Clinical Obstetrics and Gynecology, 52*(3), 441-455. https://doi.org/10.1097/GRF.0b013e3181b52930

Britton, J.R. (2011). Infant temperament and maternal anxiety and depressed mood in the early

postpartum period. *Women & Health, 51*(1), 55-71. https://doi.org/10.1080/03630242.2011.540741

Brown, T.A., Antony, M.M., & Barlow, D.H. (1992). Psychometric properties of the Penn State Worry Questionnaire in a clinical anxiety disorders sample. *Behaviour Research and Therapy, 30*(1), 33-37. https://doi.org/10.1016/0005-7967(92)90093-v

Buhr, K., & Dugas, M.J. (2002). The Intolerance of Uncertainty Scale: Psychometric properties of the English version. *Behaviour Research and Therapy,* 40(8), 931-945. https://doi.org/10.1016/s0005-7967(01)00092-4

Bunevicius, A., Kusminskas, L., & Bunevicius, R. (2020). Validity of the Edinburgh Postnatal Depression Scale. (2020). *European Psychiatry, 24*(S1), 24-E896. https://doi.org/10.1016/S0924-9338(09)71129-0

Carleton, R.N. (2012). The intolerance of uncertainty construct in the context of anxiety disorders: Theoretical and practical perspectives. *Expert Review of Neurotherapeutics, 12*(8), 937-947. https://doi.org/10.1586/ern.12.82

Carleton, R.N. (2016). Into the unknown: A review and synthesis of contemporary models involving uncertainty. *Journal of Anxiety Disorders, 39*, 30-43. https://doi.org/10.1016/j.janxdis.2016.02.007

Chin, K., Wendt, A., Bennett, I.M., & Bhat, A. (2022). Suicide and maternal mortality. *Current Psychiatry Reports, 24*(4), 239-275. https://doi.org/10.1007/s11920-022-01334-3

Counsell, A., Furtado, M., Iorio, C., Anand, L., Canzonieri, A., Fine, A., Fotinos, K., Epstein, I., & Katzman, M.A. (2017). Intolerance of uncertainty, social anxiety, and generalized anxiety: Differences by diagnosis and symptoms. *Psychiatry Research, 252*, 63-69. https://doi.org/10.1016/j.psychres.2017.02.046

Cox, J.L., Holden, J.M., & Sagovsky, R. (1987). Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry, 150,* 782-786. https://doi.org/10.1192/bjp.150.6.782

Dennis, C.L., Falah-Hassani, K., & Shiri, R. (2017). Prevalence of antenatal and postnatal anxiety: Systematic review and meta-analysis. *British Journal of Psychiatry, 210*(5), 315-323. https://doi.org/10.1192/bjp.bp.116.187179

Dole, N., Savitz, D.A., Hertz-Picciotto, I., Siega-Riz, A.M., McMahon, M.J., & Buekens, P. (2003). Maternal stress and preterm birth. *American Journal of Epidemiology, 157*(1), 14-24. https://doi.org/10.1093/aje/kwf176

Dowse, E., Chan, S., Ebert, L., Wynne, O., Thomas, S., Jones, D., Fealy, S., Evans, T.E., & Oldmeadow, C. (2020). Impact of perinatal depression and anxiety on birth outcomes: A retrospective data analysis. *Maternal and Child Health Journal, 24*, 718-726. https://doi.org/10.1007/s10995-020-02906-6

Dugas, M.J., & Ladouceur, R. (2000). Treatment of GAD. Targeting intolerance of uncertainty in two types of worry. *Behavior Modification, 24*(5), 635-657. https://doi.org/10.1177/01454455000245002

Dugas, M.J., Savard, P., Gaudet, A., Turcotte, J., Laugesen, N., Robichaud, M., Francis, K., & Koerner, N. (2007). Can the components of a cognitive model predict the severity of generalized anxiety disorder? *Behavior Therapy, 38*(2), 169-178. https://doi.org/10.1016/j.beth.2006.07.002

Dugas, M.J., Sexton, K.A., Hebert, E.A., Bouchard, S., Gouin, J.P., & Shafran, R. (2022).

Behavioral experiments for intolerance of uncertainty: A randomized clinical, trials for adults with generalized anxiety disorder. *Behavior Therapy, 53*(6), 1147-1160. https://doi.org/10.1016/j.beth.2022.05.003

Fawcett, E.J., Fairbrother, N., Cox, M.L., White, I.R., & Fawcett, J.M. (2019). The prevalence of anxiety disorders during pregnancy and the postpartum period: A multivariate Bayesian meta-analysis. *Journal of Clinical Psychiatry, 80*(4), 18r12527. https://doi.org/10.4088/JCP.18r12527

Fernandez, E., Woldgabreal, Y., Day, A., Pham, T., Gleich, B., & Aboujaoude, E. (2021). Live psychotherapy by video versus in-person: A meta-analysis of efficacy and its relationship to types and targets of treatment. *Clinical Psychology & Psychotherapy, 28*(6), 1535-1549. https://doi.org/10.1002/cpp.2594

Flink, I.K., Engström, J., Vastamäki, S., Vixner, L., & Engman, L. (2023). Expecting the uncertain: The applicability of the intolerance of uncertainty model on fear of childbirth. *Journal of Psychosomatic Obstetrics & Gynecology, 44*(1). https://doi.org/10.1080/0167482X.2023.2243648

Furtado, M., Van Lieshout, R.J., Van Ameringen, M.V., Green, S.M., & Frey, B.N. (2019). Biological and psychosocial predictors of anxiety worsening in the postpartum period: A longitudinal study. *Journal of Affective Disorders, 250*(2019), 218-225. https://doi.org/10.1016/j.jad.2019.02.064

Furtado, M., Frey, B.N., & Green, S.M. (2021). Validation of the Intolerance of Uncertainty Scale for perinatal anxiety screening. *BMC Pregnancy and Childbirth, 21,* 829. https://doi.org/10.1186/s12884-021-04296-1

Giardinelli, L., Innocenti, A., Benni, L., Stefanini, M.C., Lino, G., Lunardi, C., & Faravelli, C.

(2012). Depression and anxiety in perinatal period: Prevalence of risk factors in an Italian sample. *Archives of Women's Mental Health, 15*(1), 21-30. https://doi.org.10.1007/s00737-011-0249-8

Goldfinger, C., Green, S.M., Furtado, M., & McCabe, R.E. (2020). Characterizing the nature of worry in a sample of perinatal women with generalized anxiety disorder. *Clinical Psychology & Psychotherapy, 27*(2), 136–145. https://doi.org/10.1002/cpp.2413

Goodman, J.H., Guarino, A., Chenausky, K., Klein, L., Prager, J., Petersen, R., & Freeman, M. (2014). CALM pregnancy: Results of a pilot study of mindfulness-based cognitive therapy for perinatal anxiety. *Archives of Women's Mental Health, 17*(5), 373–387. https://doi.org/10.1007/s00737-013- 0402-7

Gratz, K.L., & Roemer, L. (2004). Multidimensional assessment of emotion regulation and dysregulation: Development, factor structure, and initial validation of the difficulties in emotion regulation scale. *Journal of Psychopathology and Behavioral Assessment, 26,* 41-54. https://doi.org/10.1023/B:JOBA.0000007455.08536.94

Green, S.M., Frey, B.N., Donegan, E., & McCabe, R.E. (2018). *Cognitive behavioural therapy for anxiety and depression during pregnancy and beyond: How to manage symptoms and maximize well-being.* Routledge.

Green, S.M., Donegan, E., McCabe, R.E., Streiner, D.L., Agako, A., & Frey, B.N. (2020). Cognitive behavioural therapy for perinatal anxiety: A randomized controlled trial. *The Australian and New Zealand Journal of Psychiatry, 54*(4), 423-432. https://doi.org/10.1177/0004867419898528

Green, S.M., Furtado, M., Inness, B.E., Frey, B.N., & McCabe, R.E. (2021). Characterizing

worry content and impact in pregnant and postpartum women with anxiety disorders during COVID-19. *Clinical Psychology & Psychotherapy, 29*(3), 1144–1157. https://doi.org/10.1002/cpp.2703

Green, S.M., Furtado, M., Inness, B.E., Frey, B.N., & McCabe, R.E. (2022). Characterizing worry content and impact in pregnant and postpartum women with anxiety disorders during COVID-19. *Clinical Psychology & Psychotherapy, 29*(3), 1144-1157. https://doi.org/10.1002/cpp.2703

Gu, Y., Gu, S., Lei, Y., & Li, H. (2020). From uncertainty to anxiety: How uncertainty fuels anxiety in a process mediated by intolerance of uncertainty. *Neural Plasticity, 22*, 8866386. https://doi.org/10.1155/2020/8866386

Hallion, L.S., Steinman, S.A., Tolin, D.F., & Diefenbach, G.J. (2018). Psychometric properties of the Difficulties in Emotion Regulation Scale (DERS) and its short forms in adults with emotional disorders. *Frontiers in Psychology, 9,* 539. https://doi.org/10.3389/fpsyg.2018.00539

Hallit, S., Haddad, C., Hallit, R., Akel, M., Obeid, S., Haddad, G., Soufia, M., Khansa, W., Khoury, R., Kheir, N., Hallit, C.A.E., & Salameh, P. (2020). Validation of the Hamilton Anxiety Rating Scale and State Trait Anxiety Inventory A and B in Arabic among the Lebanese population. *Clinical Epidemiology and Global Health, 8*(4), 1104-1109. https://doi.org/10.1016/j.cegh.2020.03.028

Hamilton, M. (1959). The assessment of anxiety states by rating. *British Journal of Medical Psychology, 32*(1), 50-55. https://doi.org/10.1111/j.2044-8341.1959.tb00467.x

Han, L., Bai, H., Lun, B., Li, Y., Wang, Y., & Ni, Q. The prevalence of fear of childbirth and its

association with intolerance of uncertainty and coping styles among pregnant Chinese women during the COVID-19 pandemic. *Frontiers in Psychiatry, 13*, 935760. https://doi.org/10.3389/fpsyt.2022.935760

Hebert, E.A. & Dugas, M.J. (2019). Behavioral experiments for intolerance of uncertainty: Challenging the unknown in the treatment of generalized anxiety disorder. *Cognitive and Behavioral Practice, 26*(2), 421-436. https://doi.org/10.1016/j.cbpra.2018.07.007

Hemant Arora, I., Woscoboinik, G.G., Mokhtar, S., Quagliarini, B., Bartal, A., Jagodnik, K.M., Barry, R.L., Edlow, A.G., Orr, S.P., & Dekel, S. (2024). Establishing validity of a diagnostic questionnaire for childbirth-related post-traumatic stress disorder. *American Journal of Obstetrics & Gynecology, 231*(1), 134.e1-134.e13. https//doi.org/10.1016/j.ajog.2023.11.1229

Hennessey, E.M.P., Swales, D.A., Markant, K., Hoffman, M.C., Hankin, B.L., & Poggi Davis, E. (2023). Maternal anxiety during pregnancy predicts infant attention to affective faces. *Journal of Affective Disorders, 344*, 104-114. https://doi.org/10.1016/j.jad.2023.09.031

Hewitt, C., Gilbody, S., Brealey, S., Paulden, S., Mann, R., Green, J., Morrell, J., Barkham, M., Light, K., & Richards, D. (2009). Methods to identify postnatal depression in primary care: An integrated evidence synthesis and value of information analysis. *Health Technology Assessment, 13*(36), 147-230. https://doi.org/10.3310/hta13360

Hofmann, S.G., Sawyer, A.T., Fang, A., & Asnaani, A. (2012). Emotion dysregulation model of mood and anxiety disorders. *Depression & Anxiety, 29*(5), 409-416. https://doi.org/10.1002/da.21888

Howard, L.M., & Khalifeh, H. (2020). Perinatal mental health: a review of progress and challenges. *World Psychiatry, 19*(3), 313-327. https://doi.org/10.1002/wps.20769

Hoyer, J., Wieder, G., Höfler, M., Krause, L., Wittchen, H.U., & Martini, J. (2020). Do lifetime anxiety disorders (anxiety liability) and pregnancy-related anxiety predict complications during pregnancy and delivery? *Early Human Development, 144*, 105022. https://doi.org/10.1016/j.earlhumdev.2020.105022

Huizink, A.C., Robles de Medina, P.G., Mulder, E.J.H., Visser, G.H.A., & Buitelaar, J.K. (2002). Psychological measures of prenatal stress as predictors of infant temperament. *Journal of the American Academy of Child & Adolescent Psychiatry, 41*(9), 1078-1085. https://doi.org/10.1097/00004583-200209000-00008

Inness, B.E., Furtado, M., Barrett, E., Stallwood, E., Streiner, D.L., McCabe, R.E., & Green, S.M. (2023). Psychometric properties of the PSWQ in a sample of pregnant and postpartum women. *Journal of Reproductive and Infant Psychology,* 1-16. https://doi.org/10.1080/02646838.2023.2209101

Irwin, J.L., Poggi Davis, E., Hobel, C.J., Coussons-Read, M., & Dunkel Schetter, C. (2020). Maternal prenatal anxiety trajectories and infant developmental outcomes in one-year-old offspring. *Infant Behavior and Development, 60*, 101468. https://doi.org/10.1016/j.infbeh.2020.101468

Johnson, S. U., Ulvenes, G., Øktedalen, T., & Hoffart, A. (2019). Psychometric properties of the general anxiety disorder 7-item (GAD-7) scale in a heterogeneous psychiatric sample. *Frontiers in Psychology, 6*(10), 1713. https://doi.org/fpsyg.2019.01713

Katz, D., Rector, N.A., & Laposa, J.M. (2017). The interaction of distress tolerance and intolerance of uncertainty in the prediction of symptom reduction across CBT for social anxiety disorder. *Cognitive Behaviour Therapy, 46*(6), 459-477. https://doi.org/10.1080/16506073.2017.1334087

Katzman, M.A., Bleau, P., Blier, P., Chokka, P., Kjernisted, K., Van Ameringen, M., Canadian Anxiety Guidelines Initiative Group on behalf of Anxiety Disorders Association of Canada/Association Canadienne des trouble anxieu and McGill University, Antony, M.M., Bouchard, S., Brunet, A., Flament, M., Grigoriadis, S., Mendlowitz, S., O'Connor, K., Rabheru, K., Richter, P.M.A., Robichaud, M., & Walker, J.R. (2014). Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders. *BMC Psychiatry, 14 Suppl 1*(Suppl 1), S1. https://doi.org/10.1186/1471-244X-14-S1-S1

Kernot, J., Olds, T., Lewis, L.K., & Maher, C. (2015). Test-retest reliability of the English version of the Edinburgh Postnatal Depression Scale. *Archives of Women's Mental Health, 18*(2), 255-257. https://doi.org/10.1007/s00737-014-0461-4

Larsen, D.L., Attkisson, C.C., Hargreaves, W.A., & Nguyen, T.D. (1979). Assessment of client/patient satisfaction: Development of a general scale. *Evaluation and Program Planning, 2*(3), 197-207. https://doi.org/10.1016/0149-0149-7189(79)90094-6

Levis, B., Negeri, Z., Sun, Y., Benedetti, A., Thombs, B.D., & DEPRESSion Screening Data (DEPRESSD) EPDS Group. (2020). Accuracy of the Edinburgh Postnatal Depression Scale (EPDS) for screening to detect major depression among pregnant and postpartum women: Systematic review and meta-analysis of individual participant data. *BMJ, 11*, 371. https://doi.org/10.1136/bmj.m4022

Littleton, H.L., Radecki Breitkopf, C., & Berenson, A.B. (2007). Correlates of anxiety symptoms during pregnancy and association with perinatal outcomes: A meta-analysis. *American Journal of Obstetrics and Gynecology, 196*(5), 424-432. https://doi.org/10.1016/j/ajog.2007.03.042

Löwe, B., Decker, O., Müller, S., Brähler, E., Schellberg, D., Herzog, W., & Herzberg, P.Y. (2008). Validation and standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the general population. *Medical Care, 46*(3), 266-274. https://doi.org/10.1097/MLR.0B013E318160D093

Maier, W., Buller, R., Philipp, M., & Heuser, I. (1988). The Hamilton Anxiety Scale: reliability, validity and sensitivity to change in anxiety and depressive disorders. *Journal of Affective Disorders, 14*(1), 61-68. https://doi.org/10.1016/0165-0327(88)90072-9

Marcotte-Beaumier, G., Bouchard, S., Gosselin, P., Langlois, F., Belleville, G., Marchand, A., & Dugas, M.J. (2021). The role of intolerance of uncertainty and working alliance in the outcome of cognitive behavioral therapy for generalized anxiety disorder delivery by videoconference: Mediation analysis. *JMIR Mental Health, 8*(3), e24541. https://doi.org/10.2196/24541

Meyer, T.J., Miller, M.L., Metzger, R.L., & Borkovec, T.D. (1990). Development and validation of the Penn State Worry Questionnaire. *Behaviour Research and Therapy, 28*(6), 487-495. https://doi.org/10.1016/0005-7967(90)90135-6

Miller, M.L., & McGuire, J.F. (2023). Targeting intolerance of uncertainty in treatment: A meta-analysis of therapeutic effects, treatment moderators, and underlying mechanisms. *Journal of Affective Disorders, 341*, 283-295. https://doi.org/10.1016/j.jad.2023.08.132

Morriss, J., Goh, K., Hirsch, C.R., & Dodd, H.F. (2023). Intolerance of uncertainty heightens negative emotional states and dampens positive emotional states. *Frontiers in Psychiatry, 14*, 1147970. https://doi.org/10.3389/fpsyt.2023.1147970

Mourady, D., Richa, S., Karam, R., Papazian, T., Moussa, F.H., Osta, N.E., Kesrouani, A.,

Azouri, J., Jabbour, H., Hajj, A., Khabbaz, L.R., & Ferri, R. (2017). Associations between quality of life, physical activity, worry, depression and insomnia: A cross-sectional designed study in health pregnant women. *PloS One, 12*(5), e0178181. https://doi.org/10.1371/journal.pone.0178181

National Institute for Health and Care Excellence. (2020). Antenatal and postnatal mental health: Clinical management and service guidance. https://www.nice.org.uk/guidance/cg192/resources/antenatal-and-postnatal-mental-health-clinical-management-and-service-guidance-pdf-35109869806789

O'Hara, M.W., & Wisner, K.L. (2014). Perinatal mental illness: Definition, description and aetiology. *Best Practice & Research Clinical Obstetrics & Gynaecology, 28*(1), 3-12. https://doi.org/10.1016/j/bpobgyn.2013.09.002

Orsolini, L., Valchera, A., Vecchiotti, R., Tomasetti, C., Iasevoli, F., Fornaro, M., De Berardis, D., Perna, G., Pompili, M., & Bellantuono, C. (2016). Suicide during perinatal period: Epidemiology, risk factors, and clinical correlates. *Frontiers in Psychiatry, 7*, 138. https://doi.org/10.3389/fpsyt.2016.00138

Pentecost, R., Latendresse, G., & Smid, M. (2021). Scoping review of the associations between perinatal substance use and perinatal depression and anxiety. *Journal of Obstetric, Gynecologic & Neonatal Nursing, 50*(4), 382-391. https://doi.org/10.1016/j.jogn.2021.02.008

Qiu, C., Williams, M.A., Calderon-Margalit, R., Cripe, S.M., & Sorensen, T.K. (2009). Preeclampsia risk in relation to maternal mood and anxiety disorders diagnosed before or during early pregnancy. *American Journal of Hypertension, 22*(4), 397-402. https://doi.org/10.1038/ajh.2008.366

Robichaud, M. (2013). Cognitive behavior therapy targeting intolerance of uncertainty: Application to a clinical case of generalized anxiety disorder. *Cognitive and Behavioral Practice. 20*(3), 251-263. https://doi.org/10.1016/j.cbpra.2012.09.001

Roddy Mitchell, A., Gordon, H., Atkinson, J., Lindquist, A., Walker, S.P., Middleton, A., Tong, S., & Hastie, R. (2023). Prevalence of perinatal anxiety and related disorders in low- and middle-income countries: A systematic review and meta-analysis. *JAMA Network Open, 6*(11), e2343711. https://doi.org/10.1001/jamanetworkopen.2023.43711

Rodriguez-Biglieri, R., & Vetere, G.L. (2011). Psychometric characteristics of the Penn State Worry Questionnaire in an Argentinean sample: A cross-cultural contribution. *The Spanish Journal of Psychology, 14*(1), 452-463. https://doi.org/10.5209/rev_sjop.2011.v14.n1.41

Rondung, E., Ekdahl, J., & Sundin, O. (2019). Potential mechanisms in fear of birth: The role of pain catastrophizing and intolerance of uncertainty. *Birth, 46*(1), 61-68. https://doi.org/10.1111/birt.12368

Ross, L.E., & McLean, L.M. (2006). Anxiety disorders during pregnancy and the postpartum period: A systematic review. *The Journal of Clinical Psychiatry, 67*(8), 1285-1298. https://doi.org/10.4088/JCP.v67n0818

Ross, K.M., Letourneau, N., Climie, E., Giesbrecht, G., & Dewey, D. (2020). Perinatal maternal anxiety and depressive symptoms and child executive function and attention at two-years of age. *Developmental Neuropsychology, 45*(6), 380-395. https://doi.org/10.1080/87565641.2020.1838525

Sahib, A., Chen, J., Cárdenas, D., & Calear, A.L. (2023). Intolerance of uncertainty and emotion

regulation: A meta-analytic and systematic review. *Clinical Psychology Review, 101*, 102270. https://doi.org/10.1016/j.cpr.2023.102270

Sani, K.R., Eeva, E., Noora, S.M., Laura, K.S., Linnea, K., & Hasse, K. (2022). The influence of maternal psychological distress on the mode of birth and duration of labor: Findings from the FinnBrain Birth Cohort Study. *Archives of Women's Mental Health, 25*, 463-472. https://doi.org/10.1007/s00737-022-01212-0

Schwarze, C.E., von der Heiden, S., Wallwiener, S., & Pauen, S. (2024). The role of perinatal maternal symptoms of depression, anxiety and pregnancy-specific anxiety for infant's self-regulation: A prospective longitudinal study. *Journal of Affective Disorders, 346*, 144-153. https://doi.org/10.1016/j.jad.2023.10.035

Shea, A., Afua Jumah, N., Forte, M., Cantin, C., Bayrampour, H., Butler, K., Francoeur, D., Green, C., & Cook, J. (2024). Guideline No. 454: Identification and treatment of perinatal mood and anxiety disorders. *Journal of Obstetrics and Gynaecology Canada, 46*(10), 102696. https://doi.org/10.1016/j.jogc.2024.102696

Shear, M.K., Vander Bilt, J., Rucci, P., Endicott, J., Lydiard, B., Otto, M.W., Pollack, M.H., Chandler, L., Williams, J., Ali, A., & Frank, D.M. (2001). Reliability and validity of a structured interview guide for the Hamilton Anxiety Rating Scale (SIGH-A). *Depression and Anxiety, 13*(4), 166-178. https://doi.org/10.1002/da/1033

Simpson, W., Glazer, M., Michalski, N., Steiner, M., & Frey, B.N. (2014). Comparative efficacy of the Generalized Anxiety Disorder 7-Item Scale and the Edinburgh Postnatal Depression Scale as screening tools for generalized anxiety disorder in pregnancy and the postpartum period. *Canadian Journal of Psychiatry, 59*(8), 434-440. https://doi.org/10.1177/070674371405900806

Sloan, E., Hall, K., Moulding, R., Bryce, S., Mildred, H., & Staiger, P.K. (2017). Emotion regulation as a transdiagnostic treatment construct across anxiety, depression, substance, eating and borderline personality disorders: A systematic review. *Clinical Psychology Review, 57*, 141-163. https://doi.org/10.1016/j.cpr.2017.09.002

Smith-Nielsen, J., Matthey, S., Lange, T., & Skovgaard Vaever, M. (2018). Validation of the Edinburgh Postnatal Depression Scale against both DSM-5 and ICD-10 diagnostic criteria for depression. *BMC Psychiatry, 18*(393), 2018. https://doi.org/10.1186/s12888-018-1965-7

Spitzer, R.L., Kroenke, K., Williams, J.B., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: The GAD-7. *Archives of Internal Medicine, 166*(10), 1092-1097. https://doi.org/10.1001/archinte.166.10.1092

Spry, E.A., Aarsman, S.R., Youssef, G.J., Patton, G.C., Macdonald, J.A., Sanson, A., Thomson, K., Hutchinson, D.M., Letcher, P., & Olsson, C.A. (2020). Maternal and paternal depression and anxiety and offspring infant negative affectivity: A systematic review and meta-analysis. *Developmental Review, 58*, 100934. https://doi.org/10.1016/j.dr.2020.100934

Stevenson, K., Fellmeth, G., Edwards, S., Calver, C., Bennett, P., Campbell, O.M.R., & Fuhr, D.C (2023). The global burden of perinatal common mental health and substance use among migrant women: a systematic review and meta-analysis. *The Lancet Public Health, 8*(3), e203-e216. https://doi.org/10.1016/S2468-2667(22)00342-5

Toscano, M., Royzer, R., Castillo, D., Li, D., & Poleshuck, E. (2021). Prevalence of depression

or anxiety during antepartum hospitalization for obstetric complications: A systematic review and meta-analysis. *Obstetrics & Gynecology, 137*(5), 881-891. https://doi.org/10.1097/AOG0000000000004335

van der Heiden, C., Muris, P., & van der Molen, H.T. (2012). Randomized controlled trial on the effectiveness of metacognitive therapy and intolerance-of-uncertainty therapy for generalized anxiety disorder. *Behaviour Research and Therapy, 50*(2), 100-109. https://doi.org/10.1016/j.brat.2011.12.005

Vigod, S.N., Frey, B.N., Clark, C.T., Grigoriadis, S., Barker, L.C., Brown, H.K., Charlebois, J., Dennis, C.L., Fairbrother, N., Green, S.M., Letourneau, N., Oberlander, T.F., Sharma, V., Singla, D.R., Steward, D.E., Bjourn, P.T., Ellington, B.D., Fleury, C., Tarasoff, L.A.,…Van Lieshout, R.J. (2025). Canadian Network for Mood and Anxiety Treatments 2024 Clinical Practice Guideline for the Management of Perinatal Mood, Anxiety, and Related Disorders: Guide de pratique 2024 du Canadian Network for Mood and Anxiety Treatments pour le traitement des troubles de l'humeur, des troubles anxieux et des troubles connexes périnatals. *The Canadian Journal of Psychiatry, 0*(0). https://doi.org/10.1177/07067437241303031

Villarreal-Zegarra, D., Paredes-Angeles, R., Mayo-Puchoc, N., Arenas-Minaya, E., Huarcaya-Victoria, J., & Copez-Lonzoy, A. (2024). Psychometric properties of the GAD-7 (General Anxiety Disorder-7): A cross-sectional study of the Peruvian general population. *BMC Psychology, 12*(183). https://doi.org/10.1186-s40359-024-01688-8

Vismara, L., Sechi, C., Neri, M., Paoletti, A., & Lucarelli, L. (2020). Maternal perinatal

depression, anxiety, fear of birth, and perception of infants' negative affectivity at three months. *Journal of Reproductive and Infant Psychology, 39*(5), 532-543. https://doi.org/10.1080/02646838.2020.1843612

Voegtline, K., Payne, J.L., Standeven, L.R., Sundel, B., Pangtey, M., & Osborne, L.M. (2021). Using the Penn State Worry Questionnaire in the peripartum. *Journal of Women's Health, 30*(12), 1761-1768. https://doi.org/10.1089/jwh.2020.8669

Vogazianos, P., Motrico, E., Domínguez-Salas, S., Christoforou, A., & Hadjigeorgiou, E. (2022). Validation of the generalized anxiety disorder screener (GAD-7) in Cypriot pregnant and postpartum women. *BMC Pregnancy Childbirth*, *22*(841). https://doi.org/10.1186/s12884-022-05127-7

Wagner Moyer, S., Ameringer, S., Elswick Jr., R.K., Nunziato, J.D., & Kinser, P.A. (2024). Exploration of the psychometric properties of the EPDS-US, a validation study. *Journal of Affective Disorders, 352,* 193-198. https://doi.org/10.1016/j.jad.2024.02.025

Weathers, F.W., Litz, B.T., Keane, T.M., Palmieri, P.A., Marx, B.P., & Schnurr, P.P. (2013). The PTSD Checklist for DSM-5 (PCL-5). Scale available from the National Center for PTSD at www.ptsd.va.gov

Weis, K.L., Walker, K.C., Chan, W., Yuan, T.T., & Lederman, R.P. (2019). Risk of preterm birth and newborn low birthweight in military women with increased pregnancy-specific anxiety. *Military Medicine, 185*(5-6), e678-e685. https://doi.org/10.1093/milmed/usz399

Wenzel, A., Haugen, E.N., Jackson, L.C., & Brendle, J.R. (2005). Anxiety symptoms and disorders at eight weeks postpartum. *Journal of Anxiety Disorders, 19*(3), 295-311. https://doi.org/10.1016/j/janxdis.2004.04.001

Whitehead, A.L., Julious, S.A., Cooper, C.L., & Campbell, M.J. (2016). Estimating the sample

size for a pilot randomized trial to minimise the overall trial sample size for the external pilot and main trial for continuous outcome variable. *Statistical Methods in Medical Research, 25*(3), 1057-1073. https://doi.org/10.1177/0962280215588241

Wilson, E.J., Abbott, M.J., & Norton, A.R. (2023). The impact of psychological treatment on intolerance of uncertainty in generalized anxiety disorder: A systematic review and meta-analysis. *Journal of Anxiety Disorders, 97,* 102729. https://doi.org/10.1016/j/janxdis.2023.102729

Womersley, K., & Alderson, H. (2024). Perinatal mental health. Medicine, 52(10), 632–636. https://doi. org/10.1016/j.mpmed.2024.07.009

World Health Organization. (2022). Guide for integration of perinatal mental health in maternal and child health services. World Health Organization. https://iris.who.int/handle/10665/362880

Zemestani, M., Beheshti, N., Rezaei, F., van der Heiden, C., & Kendall, P.C. (2021). Cognitive behavior therapy targeting intolerance of uncertainty versus selective serotonin reuptake inhibitor for generalized anxiety disorder: A randomized clinical trial. *Behaviour Change, 38*(4), 250-262. https://doi.org/10.1017/bec.2021.16

Chapter 4: Study Three

Targeting intolerance of uncertainty during pregnancy: A randomized controlled trial to prevent postpartum anxiety disorders

This article is currently under review in a peer-reviewed journal.

Furtado, M., Frey, B. N., Inness, B. E., McCabe, R. E., & Green, S. M. (2025). Targeting intolerance of uncertainty during pregnancy: A randomized controlled trial to prevent postpartum anxiety disorders. [Manuscript under review].

4.1 Abstract

Objective: Postpartum anxiety is common, often underrecognized, and associated with numerous negative outcomes for both the perinatal individual and their infant. Despite its high prevalence and burden, research focused on preventative strategies for postpartum anxiety remains very limited. This study investigated whether a six-week cognitive behavioural therapy protocol targeting intolerance of uncertainty (CBT-IU) during pregnancy could reduce risk for postpartum anxiety disorders among individuals with heightened IU.

Methods: In this investigator-initiated, single-site, proof-of-concept, randomized controlled trial (RCT; Clinicaltrials.gov ID: NCT05691140), eligible participants (n = 37) were randomized to a six-session individual CBT-IU protocol or care-as-usual (CAU). The primary objective of this study was to evaluate whether CBT-IU for pregnant individuals with elevated IU could reduce the risk of postpartum anxiety disorder, compared to care as usual (CAU). Secondary outcomes included changes in worry, depression, and emotion regulation.

Results: CBT-IU significantly reduced the risk of postpartum anxiety disorder onset compared to CAU, with none of the participants in the CBT-IU group meeting diagnostic (or provisional) criteria for an anxiety or related disorder, compared to 31.6% of participants in the CAU group. CBT-IU participants showed clinically significantly reductions in IU, worry symptoms, emotion dysregulation, and interviewer-rated anxiety symptoms compared to CAU. Treatment satisfaction among CBT-IU participants was high.

Conclusion: These findings suggest that targeting IU during pregnancy may be an effective preventive strategy for reducing the risk of postpartum anxiety disorder onset. This proof-of-concept RCT supports a large-scale RCT to ultimately test CBT-IU as an effective intervention for prevention of postpartum anxiety disorders.

4.2 Introduction

Anxiety disorders are the most common mental health conditions diagnosed during pregnancy and the postpartum (perinatal) period, with prevalence rates estimated to be between 15% to 25% (Dennis et al., 2017; Fawcett et al., 2019; Roddy Mitchell et al., 2023). The perinatal period is a time of increased psychological vulnerability (Anderson et al., 2017; Stevenson et al., 2023; Womersley & Alderson, 2024) and is associated with a range of adverse maternal and infant outcomes. Perinatal individuals with anxiety disorders are at an increased risk of obstetric complications (Dowse et al., 2020; Hoyer et al., 2020; Toscano et al., 2021; Weis et al., 2020), substance use disorders, chronic mental health difficulties, and increased suicidality (Chin et al., 2022; Dennis et al., 2017; Pentecost et al., 2021). Perinatal anxiety has also been linked to worse parent-infant bonding (O'Dea et al., 2023; Vagos et al., 2023), and poorer infant outcomes, including less secure attachment and more difficult temperament (Davies et al., 2021; Le Bas et al., 2019). Further, infants exposed to perinatal anxiety may face developmental challenges, including motor and cognitive delays, reduced attention (Hennessey et al., 2023; Irwin et al., 2020; Rogers et al., 2020; Schwarze et al., 2024; Weis et al., 2020), and increased negative affect and mental health difficulties that span from infancy to adolescence (Morales-Munoz et al., 2023; Rogers et al., 2020; Spry et al., 2020; Vismara et al., 2020).

Despite the high prevalence of anxiety disorders during the perinatal period and their associated negative outcomes, less than 20% of these individuals receive treatment (Smith et al., 2009). A key factor contributing to these low treatment rates is difficulties with accurate and early symptom detection. As a result, there has been increased attention on improving symptom detection, including efforts to identify potential risk factors. Among the more recently identified psychological risk factors of perinatal anxiety is intolerance of uncertainty (Furtado et al., 2019).

Intolerance of uncertainty (IU) is a dispositional trait characterized by the tendency to perceive uncertain situations as threatening and distressing (Carleton, 2012). IU is considered a transdiagnostic risk and maintenance factor for anxiety and related disorders, such as generalized anxiety disorder (GAD) and obsessive-compulsive disorder (Carleton, 2012; Counsell et al., 2017; Dugas & Robichaud, 2007; Gu et al., 2020; Kaçar-Başaran et al., 2023; Wilson et al., 2023). Individuals with elevated IU often experience heightened worry and engage in safety behaviours (e.g., rumination, avoidance, reassurance seeking) in an effort to reduce uncertainty (Bartoszek et al., 2022; Hebert & Dugas, 2019; Mahoney & McEvoy, 2012). Further, IU has been identified as an important mechanism in cognitive behavioural therapy (CBT) outcomes. Research suggests that reductions in IU are associated with reductions in anxiety and worry symptoms, suggesting that IU may act as both a predictor and mediator of treatment response (Bomyea et al., 2015; Marcotte-Beaumier et al., 2021; Miller & McGuire, 2023). CBT protocols specifically targeting IU have demonstrated strong effectiveness in the treatment of GAD in non-perinatal populations (Hebert & Dugas, 2019; Dugas & Ladouceur, 2000; Robichaud, 2013; van der Heiden et al., 2012; Wilson et al., 2023; Zemestani et al., 2021). More recently, studies have demonstrated that CBT for IU protocols are significantly more effective at reducing both IU and worry symptoms when compared to general CBT protocols (Wilson et al., 2023) and produce better treatment outcomes when compared to use of selective serotonin reuptake inhibitors for individuals with GAD (Zemestani et al., 2021).

The perinatal period is inherently characterized by increased uncertainty across various domains (e.g., physical health and changes, infant outcomes, transitioning to parenting). For individuals with heightened IU, this inherent uncertainty may potentially amplify distress and increase vulnerability to anxiety. Given the inherent uncertainty of the perinatal period and the

identification of IU as a risk factor for postpartum anxiety worsening, this proof-of-concept randomized controlled trial (RCT) aimed to evaluate whether a CBT protocol targeting IU during pregnancy could reduce the risk of anxiety disorders during the postpartum period. The primary objective of this study was to evaluate whether a six-session individual CBT protocol targeting IU (CBT-IU) for pregnant individuals with elevated IU could reduce postpartum anxiety disorder risk, compared to care as usual (CAU). We hypothesized that pregnant individuals with heightened IU would experience reductions in IU, as well as a decreased risk of developing an anxiety disorder in the postpartum, relative to those receiving CAU.

4.3 Methods

An investigator-initiated, single-site, proof-of-concept, RCT (Clinicaltrials.gov ID: NCT05691140) was conducted at the Women's Health Concerns Clinic (WHCC), St. Joseph's Healthcare Hamilton, a university affiliated teaching hospital clinic in Hamilton, Ontario, Canada. The study protocol was approved by the Hamilton Integrated Research Ethics Board (HiREB #13902), in accordance with the Declaration of Helsinki. All participants provided written informed consent before study entry. Please refer to Furtado et al., 2025 for a detailed description of the study protocol.

4.3.1 Participants

Eligible participants were recruited from the Greater Hamilton and surrounding area between October 2022 and August 2024. Inclusion criteria were as follows: (1) pregnant individuals (between 14 and 32 weeks' gestation); (2) 18 years or older; (3) a baseline score of 64 or greater on the IUS (Furtado et al., 2021); (4) no current psychotropic medication use or, if taking medication, no change in dose or type for a minimum of six weeks prior to baseline; (5) no concurrent psychological treatment during pregnancy (after the baseline visit); and (6) fluent

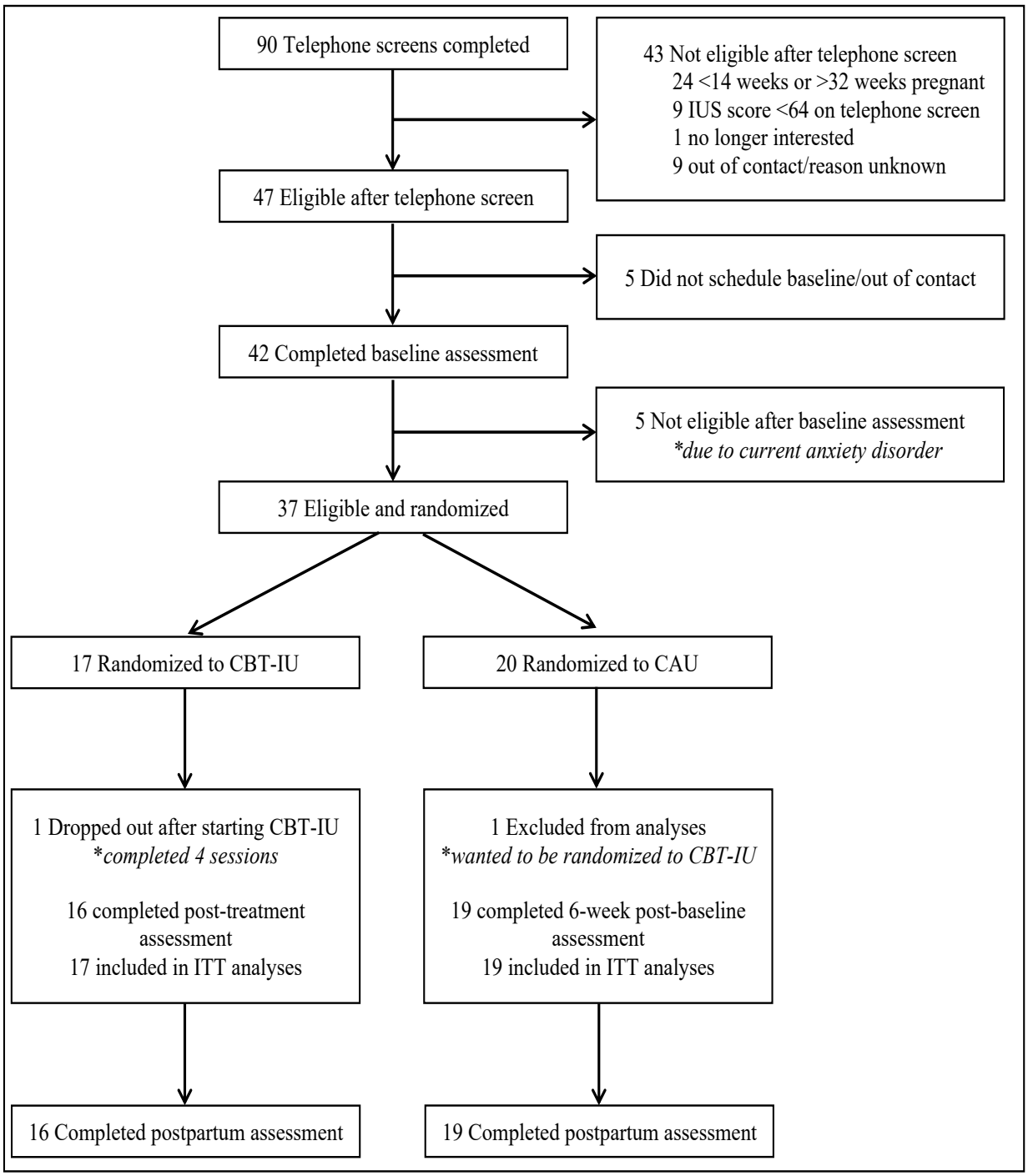
in English and able to consent for treatment. Participants were only recruited beginning as early as the second trimester of pregnancy, given that the first trimester is associated with increased risk of miscarriage, which may be associated with expected levels of greater uncertainty. Further, to allow for completion of the CBT-IU protocol prior to child delivery, participants could not be more than 32 weeks pregnant at baseline. Exclusion criteria were as follows: (1) current diagnosis of a DSM-5 (American Psychiatric Association, 2013) anxiety disorder at baseline (as assessed by the MINI); (2) current major depressive episode; (3) actively suicidal at baseline; and/or (4) diagnosed with a psychotic disorder, or current substance or alcohol use disorder. Please see **Figure 1** for a flowchart outlining participant screening, eligibility, and study procedures.

4.3.2 Study Design

Following the study screening process, participants engaged in a baseline assessment where informed consent was reviewed and provided. Psychiatric diagnoses were determined at baseline using the Mini International Neuropsychiatric Interview for DSM-5 version 7.0.1 (MINI). Participants completed the battery of interviewer-rated and self-report measures to confirm eligibility. If participants were ineligible at baseline due to an anxiety and/or mood disorder, they were offered the opportunity to receive psychological services (e.g., CBT groups) through our clinic. Eligible participants were then randomly assigned to CBT-IU (experimental condition) or CAU (control condition) using block randomization, with a computer-generated assignment sequence that was prepared prior to the start of the study. A battery of symptom assessment measures was administered within two weeks post-CBT-IU completion or within two-weeks following the control period (e.g., 6 – 8 weeks post-baseline for CAU participants), and again between 6 – 12 weeks postpartum. At the postpartum visit, the anxiety and related

disorders (e.g., obsessive-compulsive disorder, posttraumatic stress disorder) MINI modules were re-administered.

Figure 1. Flowchart of participant screening, eligibility, and study procedures.



If participants randomized to CAU exhibited clinically significant symptoms of an anxiety and/or related disorder at the post-control and/or postpartum visit(s), they were offered clinical care within the WHCC, as needed. For those randomized to CBT-IU, if clinically significant symptoms were present at the postpartum visit, the same resources would be offered. To ensure accessibility for all participants who may not have been able to attend in-person visits, all study visits were completed virtually via the Zoom Video Communications platform. To reduce attrition, all participants were compensated following each assessment time point with a $20 e-gift card.

4.3.3 Study Arms

4.3.3.1 Cognitive Behavioural Therapy Targeting Intolerance of Uncertainty for Postpartum Anxiety Prevention (CBT-IU)

Participants randomized to CBT-IU received treatment in an individual, one-to-one format with one of two trained, senior level Ph.D. clinical psychology students (MF or BEI), supervised by a licensed clinical psychologist (SMG). The CBT-IU protocol consisted of six one-hour virtual sessions that took place weekly during pregnancy and beginning within two weeks of completing their baseline assessment. Participant worksheets were developed based upon previous CBT for IU protocols used in non-perinatal populations (Dugas et al., 2022; Hebert & Dugas, 2019; Robichaud, 2013; van der Heiden et al., 2012), as well as a CBT for perinatal anxiety protocol (primary use was for perinatal anxiety psychoeducation content; Green et al., 2018). Learning of strategies was reinforced with weekly home practice exercises, which were reviewed each week with participants. Please refer to Furtado et al., 2025 for an overview of the session-by-session content.

4.3.3.2 Care As Usual (CAU)

The CAU study arm served as the control condition in this study, in which participants were not assigned to any type of study intervention. To closely resemble real world settings, participants in CAU would not be excluded from the study analyses if they initiated psychological and/or psychopharmacological treatment during the study (following baseline). Any treatments that were initiated by participants following the post-control time point were recorded at the post-control and postpartum visits. If participants in the CAU group were to experience any distressing mental health symptoms (e.g., anxiety, depression) they were asked to notify the first author to ensure that access to appropriate services were provided within the WHCC (e.g., group CBT).

4.3.4 Study Measures

The study assessment battery consisted of interviewer-rated and self-report measures of intolerance of uncertainty, anxiety, worry, and depressive symptoms, as well as measures assessing emotion regulation, traumatic stress, and treatment satisfaction. Refer to **Table 1** for a list of study measures and their associated timing.

Table 1. Schedule of study measurements.

Procedures and Measures	**Baseline**	**Post-treatment**	**Postpartum**
Enrolment			
Informed consent	X		
Randomization	X		

Structured Interview			
MINI for DSM-5	X		
Primary Outcomes			
Postpartum Anxiety Prevention[a]			X
Intolerance of Uncertainty Scale	X	X	X
Secondary Outcomes			
Hamilton Anxiety Rating Scale	X	X	X
Generalized Anxiety Disorder 7-item Scale	X	X	X
Edinburgh Postnatal Depression Scale	X	X	X
Penn State Worry Questionnaire	X	X	X
Difficulties in Emotion Regulation Scale	X	X	X
Posttraumatic Stress Disorder Checklist for DSM-5[b]	X	X	X
Client Satisfaction Questionnaire[c]		X	
Other Factors			
Demographics and Medical History	X		
Obstetric Information	X		X

[a]*Postpartum anxiety prevention is assessed through use of the anxiety and related disorders MINI modules.*

[b]*Only completed by participants endorsing a criterion A trauma at baseline or postpartum (related to traumatic childbirth).*

[c]*Only completed by participants in the CBT-IU group.*

4.3.4.1 Primary Outcomes

Postpartum Anxiety Prevention

The anxiety and related disorders MINI modules were readministered at the postpartum time point (between 6 – 12 weeks postpartum) to assess the primary outcome of postpartum anxiety prevention. Specifically, MINI diagnostic modules for anxiety disorders (e.g., generalized anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, and specific phobia), as well as anxiety-related disorders (e.g., obsessive-compulsive disorder, posttraumatic stress disorder, *in relation to traumatic childbirth experiences*) were administered. If participants were reporting other potentially relevant clinical symptoms (e.g., low mood, anhedonia), associated diagnostic modules (e.g., major depressive disorder) were administered to confirm the presence of any other DSM-5 diagnoses during postpartum. Prevention of postpartum anxiety was defined for those participants who did not meet a diagnosis of any of the aforementioned anxiety or anxiety-related disorders at the postpartum time point. Given the length of symptom duration (i.e., minimum of six months) necessary to meet diagnostic criteria for specific anxiety disorders (e.g., GAD, agoraphobia, specific phobia) we used *provisional* diagnostic criteria as participants were followed up to 12 weeks postpartum. Specifically, participants must have fulfilled all other DSM-5 criteria, particularly whether symptoms experienced were significantly distressing and/or impairing functioning, to meet for a provisional postpartum diagnosis of such disorders.

Intolerance of Uncertainty Scale

The 27-item Intolerance of Uncertainty Scale (IUS; Buhr & Dugas, 2002; Freeston et al., 1994) is a self-report measure of IU, a key feature of anxiety disorders. Items are scored on a 5-point Likert scale (1 = not at all to 5 = entirely characteristic), with higher total scores indicating

greater difficulties tolerating uncertainty. The IUS has demonstrated excellent internal consistency ($\alpha = 0.91 – 0.95$) and good test-retest reliability ($r = 0.78$) in non-perinatal populations (Buhr & Dugas, 2002; Freeston et al., 1994). Within a perinatal population, the IUS demonstrated strong psychometric properties ($\alpha = 0.95$; $r = 0.91$), with an optimal clinical cut-off score of 64 or greater yielding 89% sensitivity and 65% specificity, and very good positive (79%) and negative (80%) predictive values (Furtado et al., 2021).

4.3.4.2 Secondary Outcomes

Hamilton Anxiety Rating Scale

The Hamilton Anxiety Rating Scale (HAM-A; Hamilton, 1959) is a 14-item, interviewer-administered tool designed to assess overall anxiety severity and is widely recognized as a gold-standard measure. Both psychic (e.g., fear, psychological distress) and somatic (e.g., physical sensations) anxiety symptoms are assessed with the HAM-A. Each item is rated on a 4-point Likert scale, with higher scores reflecting greater symptom severity. The HAM-A has demonstrated strong psychometric properties, including excellent internal consistency ($\alpha = 0.82–0.92$) and test-retest reliability ($r = 0.89$) in populations with anxiety and depression (Hallit et al., 2020; Shear et al., 2001), and has been used in perinatal populations (Furtado et al., 2019; Green et al., 2020; Guo et al., 2022).

Generalized Anxiety Disorder 7-Item Scale

The Generalized Anxiety Disorder 7-Item Scale (GAD-7; Spitzer et al., 2006) is a self-report measure assessing anxiety severity over the past two weeks using a 4-point Likert scale (0 = not at all to 3 = nearly every day). The GAD-7 has shown excellent internal consistency ($\alpha = 0.88–0.93$; Johnson et al., 2019; Spitzer et al., 2006; Villarreal-Zegarra, 2024) and strong test-retest reliability (Spitzer et al., 2006) in non-perinatal populations. The scale is also validated for

perinatal populations, with acceptable sensitivity (61.3%) and specificity (72.7%) when using a clinical cut-off score of 13 or greater (Simpson et al., 2014).

Edinburgh Postnatal Depression Scale

The Edinburgh Postnatal Depression Scale (EPDS; Cox et al., 1987) is a 10-item self-report measure of perinatal depression symptoms, with higher total scores indicating greater symptom severity. The EPDS has demonstrated good internal consistency (α = 0.82–0.83; Bunevicius et al., 2020; Wagner Moyer et al., 2024) and test-retest reliability (ICC = 0.92; Kernot et al., 2015). A clinical cut-off score of 11 or greater has been more recently recommended for optimal sensitivity (81%) and specificity (88%; Levis et al., 2020), over the more commonly and previously used cut-off of 13 or greater (Hewitt et al., 2009).

Penn State Worry Questionnaire

The Penn State Worry Questionnaire (PSWQ; Meyer et al., 1990) is a 16-item self-report measure of pathological worry. Items are rated on a 5-point Likert scale (1 = not at all typical of me to 5 = very typical of me), with higher scores reflecting greater worry symptoms. The PSWQ has demonstrated excellent internal consistency (α = 0.92–0.95; Inness et al., 2023; Rodriguez-Biglieri & Vetere, 2011; Voegtline et al., 2021) and strong test-retest reliability (r = 0.82–0.92; Meyer et al., 1990; Rodriguez-Biglieri & Vetere, 2011). It has been used extensively in perinatal research (e.g., Goodman et al., 2014; Green et al., 2020, 2021; Inness et al., 2023).

Difficulties in Emotion Regulation Scale

The Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004) is a 36-item self-report measure assessing six emotion regulation dimensions: non-acceptance, goals, impulse, awareness, strategies, and clarity. Items are rated on a 5-point Likert scale ranging from 1 (almost never) to 5 (almost always), with higher scores indicating greater difficulties in

emotion regulation. The DERS has shown good internal consistency (α = 0.82–0.94) and test-retest reliability (r = 0.88) in both non-perinatal and perinatal populations (Gratz & Roemer, 2004; Barrett et al., 2023).

Posttraumatic Stress Disorder Checklist for DSM-5

The Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5; Weathers et al., 2013) is a 20-item self-report measure assessing posttraumatic stress disorder (PTSD) symptoms. Items are rated on a 5-point Likert scale (0 = not at all to 4 = extremely), with a suggested clinical cut-off score of 33 or greater for PTSD. The PCL-5 demonstrates excellent internal consistency (α = 0.94–0.96), test-retest reliability (r = 0.82–0.86), and strong convergent and discriminant validity (Bovin et al., 2016). It has also been validated in postpartum populations, particularly for PTSD related to traumatic childbirth (α = 0.93; Hemant Arora et al., 2024). In present study, the PCL-5 was only administered to participants who reported a Criterion A trauma at baseline or postpartum (e.g., traumatic childbirth).

4.3.4.3 Client Satisfaction with Treatment

Client Satisfaction Questionnaire

The Client Satisfaction Questionnaire (CSQ; Larsen et al., 1979) is an 8-item self-report measure assessing client satisfaction with health services. Items are rated on a 4-point Likert scale (1–4), with higher total scores reflecting greater satisfaction with services. The CSQ has shown excellent internal consistency (α = 0.92–0.93) and has been used in perinatal studies to assess client satisfaction with the received intervention (Green et al., 2020; Thomas et al., 2014). Only participants assigned to CBT-IU completed the CSQ to assess satisfaction with the treatment protocol.

4.3.4.4 Other Factors

Demographics and Medical History

Information pertaining to participant's age, gender identity, race, marital status, parity, education level, and current medications were collected at baseline. At the postpartum visit, participants were asked about medication use, as well as whether they had engaged in any psychotherapeutic interventions during the postpartum period, and these were added as covariates to the analyses.

Obstetric Information

At the baseline visit, participants were asked about their planned method of delivery (e.g., vaginal, caesarian section) and at the baseline visit. At the postpartum visit, information was collected pertaining to the participant's actual method of delivery, whether there were any birth and/or delivery complications (e.g., pre-term birth, NICU admission, etc.).

4.3.5 Statistical Analysis

Participants in CBT-IU and CAU were compared on baseline clinical and demographic characteristics using chi square (χ^2) or independent sample t-tests. To assess the primary outcome of postpartum anxiety prevention, a chi-square test was used to compare the proportion of participants meeting diagnostic (or provisional) criteria for an anxiety and/or related disorder between CBT-IU and CAU. A modified intention-to-treat (ITT) approach was used, in which participants who did not complete any self-report baseline measures were excluded (n = 1). Linear mixed models (LMMs) were used to examine changes in outcomes over time between CBT-IU and CAU, where the model included fixed effects for group (CBT-IU vs. CAU), time (e.g., baseline, post-treatment/control, postpartum), and their interaction (group x time). Medication use for mental health concerns and psychotherapy use during the postpartum were

included as a covariate. Partial eta-squared (η^2_p) were computed to estimate effect sizes. All statistical tests were two-tailed with a significance level set a $p<0.05$. Statistical analyses were conducted using IBM SPSS Statistics (version 29).

4.4 Results

A total of 42 participants completed the study baseline screening assessment, five of which were deemed ineligible due to meeting current diagnostic criteria for a DSM-5 anxiety disorder. Following randomization of our 37 participants, one participant randomized to CAU declined further participation (due to wanting to be randomized to CBT-IU) and did not complete the baseline self-report measures (aside from the IUS used to determine eligibility) and as such, they were excluded from the analyses. This resulted in a modified ITT sample of 36 participants (Mean age = 32.4, SD = 3.5, range = 25 to 38). One participant in the CBT-IU group discontinued participation in the study following four CBT-IU sessions, due to a family emergency that prevented them from actively engaging. As such, they were unable to complete the remaining study visits, including the postpartum visit in which we assessed for anxiety and related disorders. This participant was therefore excluded from our primary outcome (postpartum anxiety disorder) analyses, as we were unable to assess for the presence of any anxiety and/or related disorders in the postpartum period. There were no significant differences between groups on baseline demographic and clinical characteristics (**see Table 2**). At the postpartum timepoint, no participants endorsed a criterion A index trauma related to childbirth.

Table 2. Baseline demographic and clinical characteristics by group.

Baseline characteristics	**CBT-IU (*n* = 17)**	**CAU (*n* = 20)**	***p* value (t/χ^2)**
Age, mean (SD), years	31.43 (2.74)	33.11 (3.91)	0.18

Race			
Black	0 (0)	2 (10)	
East Asian	0 (0)	2 (10)	
South Asian	0 (0)	1 (5)	0.21
West Asian	1 (5.9)	0 (0)	
White	16 (94.1)	15 (75)	
Marital status			
Single	0 (0)	2 (10)	0.25
Married	16 (94.1)	15 (75)	
Common-law	1 (5.9)	3 (15)	
Education level			
High school	0 (0)	2 (10)	
College/diploma	4 (23.5)	0 (0)	0.08
University/degree	7 (41.2)	8 (40)	
Postgraduate	6 (35.3)	10 (50)	
Parity			
Primigravida	10 (58.8)	11 (55)	0.82
Multigravida	7 (41.2)	9 (45)	

Data are presented as *n* (%) of participants, unless otherwise indicated. *t* = t-test; χ^2 = chi-square test of difference between groups; CBT-IU: Cognitive Behavioural Therapy for Intolerance of Uncertainty; CAU: Care-as-usual; SD: standard deviation

4.4.1 Primary Outcomes

A chi-square test of independence was conducted to examine the relationship between groups (CBT-IU and CAU) and postpartum outcome (presence of anxiety and/or related disorder). The results indicated that there was a significant relationship between group and postpartum outcome [χ^2 (1, N = 35) = 6.098, p = 0.014] suggesting that participants in the CAU group were significantly more likely to meet criteria for an anxiety disorder during the postpartum period compared to participants in the CBT-IU group. Of the 16 CBT-IU participants who completed their postpartum assessment, none (0%) met diagnostic criteria for an anxiety and/or related disorder. One (6.3%) CBT-IU participant met criteria for current Major Depressive Disorder, peripartum onset, and was offered services within our clinic. Of the 19 CAU participants, six (31.6%) met diagnostic (or provisional) criteria for an anxiety disorder. Specifically, two participants met diagnostic criteria for Social Anxiety Disorder and four met provisional diagnostic criteria for GAD in the postpartum. Of the CAU participants meeting diagnostic (or provisional) criteria for an anxiety disorder, three had begun medication or psychotherapy specific for anxiety occurring in the postpartum. All were offered services (e.g., CBT group for perinatal anxiety) within our clinic. The CBT-IU group also exhibited significantly greater reductions in IU [IUS; F (2, 66.97) = 6.53, p = 0.003, η^2_p = 0.16] both following completion of CBT-IU and at the 6 – 12 week postpartum visit, as compared to CAU (**Table 3**).

4.4.2 Secondary Outcomes

There were significantly greater reductions in the CBT-IU group for self-reported worry [PSWQ; F (2, 66.40) = 9.47, p <0.001, η^2_p = 0.22], and emotion dysregulation symptoms [DERS; F (2, 66.39) = 4.27, p = 0.018, η^2_p = 0.11] compared to CAU. There were no significant

differences between groups in self-reported anxiety (GAD-7) and depressive (EPDS) symptoms. With respect to interviewer-rated anxiety (HAM-A), there was a significantly greater reduction in anxiety symptoms in CBT-IU compared to CAU [F (2, 67.35) = 12.76, p <0.001, η^2_p = 0.28] (**Table 3**).

4.4.3 Treatment Satisfaction

Participants in CBT-IU were highly satisfied with the treatment received (CSQ, Mean = 29.73, SD = 3.15). All CBT-IU participants rated the treatment as 'excellent' (86.7%) or 'good' (13.3%). Participants also reported that CBT-IU helped them cope 'better' (33.3%) or a 'great deal better' (66.7%) with their symptoms, and participants reported being 'very satisfied' (73.3%) or 'mostly satisfied' (26.7%) with the treatment. All participants (100%) reported that they would recommend CBT-IU to others.

Table 3. Linear mixed model comparing CBT-IU (n=16) to Care as Usual (n=19) on outcomes from baseline to postpartum.

	CBT-IU			**CAU**						
	Baseline Mean (SD)	***Post-tx Mean (SD)***	***Postpartum Mean (SD)***	***Baseline Mean (SD)***	***Post-CAU Mean (SD)***	***Postpartum Mean (SD)***		***F*-value**	***p*-value**	η^2_p
IUS	82 (9.9)	64.5 (20.5)	64.9 (19.5)	75.5 (10.9)	71.4 (13.9)	69.9 (18.3)	Time Group x Time	11.93 6.53	<0.001 0.003	0.16
HAM-A	11.7 (4.8)	7.4 (4.4)	5.7 (2.6)	9.5 (3.9)	14.32(5.5)	9.95 (4.1)	Time Group x Time	5.52 12.76	0.006 <0.001	0.28
PSWQ	60 (7.8)	50.4 (7.4)	51.3 (11.5)	58.1 (7.1)	59.1 (7.2)	57 (9.8)	Time Group x Time	7.03 9.47	0.002 <0.001	0.22
GAD-7	8 (4.2)	5.3 (2.7)	5.6 (4.4)	7.6 (3.9)	7.7 (3.9)	6.9 (5.4)	Time Group x Time	1.41 2.23	0.251 0.115	0.06
EPDS	8.19 (3.4)	7.31 (3.9)	5.69 (3.3)	8.74 (4.9)	8.95 (4.5)	7.42 (4.)	Time Group x Time	2.25 0.44	0.113 0.645	0.01
DERS	84.4 (14.5)	73.7 (14.2)	67.1 (17.1)	86.4 (18.9)	83.8 (14.8)	81.84 (18.3)	Time Group x Time	6.58 4.27	0.002 0.018	0.11

4.5 Discussion

Anxiety disorders during the perinatal period are common, often underrecognized, and associated with numerous adverse outcomes for both the perinatal individual and infant. To date, most of the research has focused on the use of interventions in which anxiety is addressed after symptoms have emerged and led to clinical distress and impairments in day-to-day functioning, with little to no research focusing on preventing anxiety disorders before they develop. The aim of the present study was to evaluate the effectiveness of a CBT protocol targeting IU for reducing the risk of postpartum anxiety disorder onset. Given that IU has been consistently linked to the onset and maintenance of anxiety disorders (Carleton, 2012; Counsell et al., 2017; Dugas & Robichaud, 2007; Gu et al., 2020; Wilson et al., 2023), and was more recently identified as a risk factor for postpartum anxiety worsening (Furtado et al., 2019), we hypothesized that reducing IU during pregnancy could lower the risk of developing an anxiety disorder during the postpartum period. Our findings provide initial evidence for this hypothesis, as none of the participants in the CBT-IU group met diagnostic (or provisional) criteria for an anxiety or related disorder in the postpartum, compared to 31.6% of participants in the CAU group. Additionally, participants in CBT-IU experienced significantly greater reductions in IU compared to those in CAU at both the post-treatment and postpartum follow-up visits. These group differences are clinically meaningful and suggest that targeting IU during pregnancy may reduce the likelihood of developing an anxiety disorder in the postpartum, a period known to be associated with increased vulnerability to mental health difficulties (Anderson et al., 2017; Ross & McLean, 2006; Stevenson et al., 2023; Womersley & Alderson, 2024).

CBT-IU was also associated with significantly greater reductions in worry symptoms, as measured by the PSWQ. Research has shown that IU is highly associated with worry in both

clinical and non-clinical populations and both share common features regarding uncertainty and uncertainty-induced safety behaviours (Bomyea et al., 2015; Buhr & Dugas, 2002; Gu et al., 2020). CBT-IU was aimed at helping individuals recognize and reframe unhelpful beliefs about uncertainty (e.g., uncertain situations lead to negative outcomes), better tolerate uncertainty, and therefore reduce reliance on excessive worry and rumination as potential coping strategies. By learning to respond to uncertainty with greater flexibility, tolerance, and less avoidance and rumination, participants may have been less likely to experience distressing worry, including in the postpartum period, when more uncertainly naturally exists. Participants in the CBT-IU group also exhibited significantly greater reductions in interviewer-rated anxiety symptom severity, as measured by the HAM-A. Through CBT-IU strategies, such as behavioural experiments and imaginal exposure, participants repeatedly practice tolerating uncertainty and learn that worry and excessive safety behaviours are not necessary to prevent negative outcomes. As such, participants likely experienced both cognitive and somatic anxiety reductions, both of which are captured with the HAM-A. These findings align with prior research demonstrating that IU is a predictor and mediator of CBT treatment response, specifically in relation to reduction in worry and anxiety symptoms (Bomyea et al., 2015; Marcotte-Beaumier et al., 2021; Miller & McGuire, 2023). Interestingly, group differences did not emerge for self-reported anxiety (GAD-7), despite significant differences between groups on the HAM-A. This discrepancy may reflect differences in how these measures assess anxiety symptoms. The HAM-A captures a broader spectrum of anxiety symptoms, including both cognitive and somatic features, such as physical symptoms related to anxiety (e.g., cardiovascular, gastrointestinal). Individuals with increased IU tend to experience greater autonomic arousal in uncertain situations (Morriss et al., 2024), which may be better captured by the HAM-A, as it assesses a broader range of anxiety symptoms compared to

the GAD-7. As such, the GAD-7 may be less sensitive to the somatic symptoms of anxiety, which could help explain why significant group differences were observed on the HAM-A, but not the GAD-7.

Emotion dysregulation also significantly decreased in the CBT-IU group compared to CAU, as measured by the DERS. Emotion dysregulation is a known transdiagnostic factor in the development and maintenance of anxiety disorders (Blay et al., 2024; Sloan et al., 2017), and recent research has also demonstrated its role in the perinatal period and association to perinatal anxiety (Agako et al., 2021). Individuals with greater IU interpret uncertain situations as threatening, which can heighten anxiety and reliance on maladaptive emotion regulation strategies, such as reassurance-seeking and thought suppression (Sahib et al., 2024). By targeting IU directly, CBT-IU may reduce the perceived threat of uncertainty, thereby decreasing the need for unhelpful emotion regulation strategies. As individuals build greater tolerance for uncertainty and the distress it evokes, they may be become better equipped to engage in flexible and adaptive responses, in place of maladaptive emotion regulation strategies. This may explain why CBT-IU was more effective than CAU in reducing emotion dysregulation. Although CBT-IU was effective in reducing IU, anxiety, worry, and emotion dysregulation, it did not lead to significant reductions in depression scores (EPDS) compared to CAU. One likely explanation is that the CBT-IU protocol did not directly target depression symptoms, as it focused primarily on addressing IU. Additionally, baseline depression scores in our sample were relatively low, which may have limited the potential for observable changes. Lastly, high treatment satisfaction among CBT-IU participants further underscores its feasibility and acceptability. All participants endorsed the treatment as helpful, with the majority rating it as “excellent” and stating that they would recommend it to others. These results suggest that pregnant individuals with heightened

IU who may be at risk of postpartum anxiety are not only willing to engage in a brief intervention but also perceive it as valuable and effective.

4.5.1 Limitations

There are some limitations that should be considered when interpreting these findings. The sample size was relatively small and primarily composed of individuals from similar demographic backgrounds, which may limit generalizability. As this was a proof-of-concept trial, we were interested in determining any initial evidence of effectiveness of CBT-IU in reducing risk of postpartum anxiety disorder onset. The follow-up period was limited to 6 – 12 weeks postpartum, and therefore longer-term outcomes remain unknown. Additionally, given the timeline we used provisional diagnostic criteria for certain DSM-5 anxiety disorders (e.g., GAD) and as such, we do not know whether full diagnostic criteria that includes the minimum 6-month duration of symptoms would be met if participants were followed. While standardized procedures were used, a limitation of this study is that assessors were not blinded to group allocation, which may have introduced a potential risk of unconscious bias. Future larger, blinded trials with additional postpartum timepoints (e.g., 6 months, 12 months postpartum) are needed to confirm the effectiveness of CBT-IU for preventing anxiety disorders during the postpartum. Additionally, while CAU served as the comparison condition, it is not known whether CBT-IU's benefits were due to its specific components or the structured support it provided. Future studies would benefit from a comparison of CBT-IU to other forms of structured support (e.g., psychoeducation) that do not include active CBT-IU components.

4.6 Conclusion

Although postpartum anxiety is associated with a range of negative outcomes for both the individual and their infant, research to date has not focused on preventative interventions for

those at increased risk of developing anxiety disorders during the postpartum period. This study provides initial evidence that targeting IU through a brief CBT protocol during pregnancy may reduce the risk of developing anxiety disorders in postpartum individuals with elevated IU during pregnancy. These findings underscore the potential of targeting psychological vulnerability factors, such as IU, to prevent the onset of anxiety during the postpartum, which is already a time marked by increased uncertainty and vulnerability. This study highlights the value of promoting prevention by providing support and tools to perinatal individuals who are at risk of developing an anxiety disorder, rather than waiting until symptoms become significantly distressing and interfering.

4.7 Declarations

Funding

This study was funded by an unrestricted educational gift from Shoppers Drug Mart (Run for Women) and in-kind by the Women's Health Concerns Clinic, St. Joseph's Healthcare Hamilton.

Acknowledgements

We would like to thank all the perinatal individuals who participated in this study for their time and contribution, this work would not be possible without you. We also thank Meagan Tamburro for her assistance with recruitment for this study.

References

Agako, A., Donegan, E., McCabe, R.E., Frey, B.N., Streiner, D., & Green, S. (2021). The role of emotion dysregulation in cognitive behavioural group therapy for perinatal anxiety: Results from a randomized controlled trial and routine clinical care. *Journal of Affective Disorders, 292*, 517-525. https://doi.org/10.1016/j.jad.2021.05.084

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). American Psychiatric Association Publishing.

Anderson, F.M., Hatch, S.L., Comacchio, C., & Howard, L.M. (2017). Prevalence and risk of mental disorders in the perinatal period among migrant women: A systematic review and meta-analysis. *Archives of Women's Mental Health, 20*(3), 449-462. https://doi.org/10.1007/s00737-017-0723-z

Barrett, E.N., Frey, B.N., Streiner, D.L, Agako, A., Inness, B.E., Furtado, M., Caropreso, L., & Green, S.M. (2023). Psychometric properties of the Difficulties in Emotion Regulation Scale in a perinatal sample. *Journal of Reproductive and Infant Psychology,* 1-20. https://doi.org/10.1080/02646838.2023.2227648

Bartoszek, G., Ranney, R.M., Curanovic, I., Costello, S.J., & Behar, E. (2022). Intolerance of uncertainty and information-seeking behavior: Experimental manipulation of threat relevance. *Behaviour Research and Therapy, 154,* 104125. https://doi.org/10.1016/j.brat.2022.104125

Blay, M., Duarte, M., Dessouli, M.A., Durpoix, A., Rüfenacht, E., Weibel, S., Speranza, M., & Perroud, N. (2024). Proposition of a transdiagnostic processual approach of emotion dysregulation based on core triggers and interpersonal styles. *Frontiers in Psychiatry, 15*, 1260138. https://doi.org/10.3389/fpsyt.2024.1260138

Bomyea, J., Ramsawh, H., Ball, T.M., Taylor, C.T., Paulus, M.P., Lang, A.J., & Stein, M.B. (2015). Intolerance of uncertainty as a mediator of reductions in worry in a cognitive behavioural treatment program for generalized anxiety disorder. *Journal of Anxiety Disorders, 33,* 90-94. https://doi.org/10.1016/j.janxdis.2015.05.004

Bovin, M.J., Marx, B.P., Weathers, F.W., Gallagher, M.W., Rodriguez, P., Schnurr, P.P., & Keane, T.M. (2016). Psychometric properties of the PTSD Checklist for Diagnostic and Statistical Manual of Mental Disorders—Fifth Edition (PCL-5) in veterans. *Psychological Assessment*, *28*(11), 1379-1391. https://doi.org/10.1037/pas0000254

Buhr, K., & Dugas, M.J. (2002). The Intolerance of Uncertainty Scale: Psychometric properties of the English version. *Behaviour Research and Therapy,* 40(8), 931-945. https://doi.org/10.1016/s0005-7967(01)00092-4

Bunevicius, A., Kusminskas, L., & Bunevicius, R. (2020). Validity of the Edinburgh Postnatal Depression Scale. (2020). *European Psychiatry, 24*(S1), 24-E896. https://doi.org/10.1016/S0924-9338(09)71129-0

Carleton, R.N. (2012). The intolerance of uncertainty construct in the context of anxiety disorders: Theoretical and practical perspectives. *Expert Review of Neurotherapeutics, 12*(8), 937-947. https://doi.org/10.1586/ern.12.82

Chin, K., Wendt, A., Bennett, I.M., & Bhat, A. (2022). Suicide and maternal mortality. *Current Psychiatry Reports, 24*(4), 239-275. https://doi.org/10.1007/s11920-022-01334-3

Counsell, A., Furtado, M., Iorio, C., Anand, L., Canzonieri, A., Fine, A., Fotinos, K., Epstein, I., & Katzman, M.A. (2017). Intolerance of uncertainty, social anxiety, and generalized https://doi.org/10.1016/j.psychres.2017.02.046

Cox, J.L., Holden, J.M., & Sagovsky, R. (1987). Detection of postnatal depression: Development

of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry, 150,* 782-786. https://doi.org/10.1192/bjp.150.6.782

Davies, S.M., Silverio, S.A., Christiansen, P., & Fallon, V. (2021). Maternal-infant bonding and perceptions of infant temperament: The mediating role of maternal mental health. *Journal of Affective Disorders, 282*, 1323-1329. https://doi.org/10.1016/j.jad.2021.01.023

Dennis, C.L., Falah-Hassani, K., & Shiri, R. (2017). Prevalence of antenatal and postnatal anxiety: Systematic review and meta-analysis. *British Journal of Psychiatry, 210*(5), 315-323. https://doi.org/10.1192/bjp.bp.116.187179

Dowse, E., Chan, S., Ebert, L., Wynne, O., Thomas, S., Jones, D., Fealy, S., Evans, T.E., & Oldmeadow, C. (2020). Impact of perinatal depression and anxiety on birth outcomes: A retrospective data analysis. *Maternal and Child Health Journal, 24*, 718-726. https://doi.org/10.1007/s10995-020-02906-6

Dugas, M.J., & Ladouceur, R. (2000). Treatment of GAD. Targeting intolerance of uncertainty in two types of worry. *Behavior Modification, 24*(5), 635-657. https://doi.org/10.1177/01454455000245002

Dugas, M.J., & Robichaud, M. (2007). *Cognitive-behavioral treatment for generalized anxiety disorder: From science to practice.* Routledge/Taylor & Francis Group.

Dugas, M.J., Sexton, K.A., Hebert, E.A., Bouchard, S., Gouin, J.P., & Shafran, R. (2022). Behavioral experiments for intolerance of uncertainty: A randomized clinical, trials for adults with generalized anxiety disorder. *Behavior Therapy, 53*(6), 1147-1160. https://doi.org/10.1016/j.beth.2022.05.003

Fawcett, E.J., Fairbrother, N., Cox, M.L., White, I.R., & Fawcett, J.M. (2019). The prevalence of

anxiety disorders during pregnancy and the postpartum period: A multivariate Bayesian meta-analysis. *Journal of Clinical Psychiatry, 80*(4), 18r12527. https://doi.org/10.4088/JCP.18r12527

Freeston, M. H., Rhéaume, J., Letarte, H., Dugas, M. J., & Ladouceur, R. (1994). Why do people worry? *Personality and Individual Differences, 17,* 791-802. https://doi.org/10.1016/0191- 8869(94)90048-5

Furtado, M., Van Lieshout, R.J., Van Ameringen, M.V., Green, S.M., & Frey, B.N. (2019). Biological and psychosocial predictors of anxiety worsening in the postpartum period: A longitudinal study. *Journal of Affective Disorders, 250*(2019), 218-225. https://doi.org/10.1016/j.jad.2019.02.064

Furtado, M., Frey, B.N., & Green, S.M. (2021). Validation of the Intolerance of Uncertainty Scale for perinatal anxiety screening. *BMC Pregnancy and Childbirth, 21,* 829. https://doi.org/10.1186/s12884-021-04296-1

Furtado, M., Frey, B.N., Inness, B.E., McCabe, R.E., & Green, S.M. (2025). Cognitive behavioural therapy for intolerance of uncertainty: A study protocol for the prevention of postpartum anxiety. *Journal of Reproductive and Infant Psychology,* 1-20. Advance online publication. https://doi.org/10.1080/02646838.2025.2495928

Goodman, J.H., Guarino, A., Chenausky, K., Klein, L., Prager, J., Petersen, R., & Freeman, M. (2014). CALM pregnancy: Results of a pilot study of mindfulness-based cognitive therapy for perinatal anxiety. *Archives of Women's Mental Health, 17*(5), 373–387. https://doi.org/10.1007/s00737-013- 0402-7

Gratz, K.L., & Roemer, L. (2004). Multidimensional assessment of emotion regulation and

dysregulation: Development, factor structure, and initial validation of the difficulties in emotion regulation scale. *Journal of Psychopathology and Behavioral Assessment, 26,* 41-54. https://doi.org/10.1023/B:JOBA.0000007455.08536.94

Green, S.M., Frey, B.N., Donegan, E., & McCabe, R.E. (2018). *Cognitive behavioural therapy for anxiety and depression during pregnancy and beyond: How to manage symptoms and maximize well-being.* Routledge.

Green, S.M., Donegan, E., McCabe, R.E., Streiner, D.L., Agako, A., & Frey, B.N. (2020). Cognitive behavioural therapy for perinatal anxiety: A randomized controlled trial. *The Australian and New Zealand Journal of Psychiatry, 54*(4), 423-432. https://doi.org/10.1177/0004867419898528

Green, S.M., Furtado, M., Inness, B.E., Frey, B.N., & McCabe, R.E. (2021). Characterizing worry content and impact in pregnant and postpartum women with anxiety disorders during COVID-19. *Clinical Psychology & Psychotherapy, 29*(3), 1144–1157. https://doi.org/10.1002/cpp.2703

Gu, Y., Gu, S., Lei, Y., & Li, H. (2020). From uncertainty to anxiety: How uncertainty fuels anxiety in a process mediated by intolerance of uncertainty. *Neural Plasticity, 2020*, 8866386. https://doi.org/10.1155/2020/8866386

Guo, X., Guo, X., Wang, R., & Zhang, Y. (2022). Effects of Perinatal Cognitive Behavioral Therapy on Delivery Mode, Fetal Outcome, and Postpartum Depression and Anxiety in Women. *Computational and Mathematical Methods in Medicine*, *2022*, 8304405. https://doi.org/10.1155/2022/8304405

Hallit, S., Haddad, C., Hallit, R., Akel, M., Obeid, S., Haddad, G., Soufia, M., Khansa, W.,

Khoury, R., Kheir, N., Hallit, C.A.E., & Salameh, P. (2020). Validation of the Hamilton Anxiety Rating Scale and State Trait Anxiety Inventory A and B in Arabic among the Lebanese population. *Clinical Epidemiology and Global Health, 8*(4), 1104-1109. https://doi.org/10.1016/j.cegh.2020.03.028

Hamilton, M. (1959). The assessment of anxiety states by rating. *British Journal of Medical Psychology, 32*(1), 50-55. https://doi.org/10.1111/j.2044-8341.1959.tb00467.x

Hebert, E.A. & Dugas, M.J. (2019). Behavioral experiments for intolerance of uncertainty: Challenging the unknown in the treatment of generalized anxiety disorder. *Cognitive and Behavioral Practice, 26*(2), 421-436. https://doi.org/10.1016/j.cbpra.2018.07.007

Hemant Arora, I., Woscoboinik, G.G., Mokhtar, S., Quagliarini, B., Bartal, A., Jagodnik, K.M., Barry, R.L., Edlow, A.G., Orr, S.P., & Dekel, S. (2024). Establishing validity of a diagnostic questionnaire for childbirth-related post-traumatic stress disorder. *American Journal of Obstetrics & Gynecology, 231*(1), 134.e1-134.e13. https//doi.org/10.1016/j.ajog.2023.11.1229

Hennessey, E.M.P., Swales, D.A., Markant, K., Hoffman, M.C., Hankin, B.L., & Poggi Davis, E. (2023). Maternal anxiety during pregnancy predicts infant attention to affective faces. *Journal of Affective Disorders, 344*, 104-114. https://doi.org/10.1016/j.jad.2023.09.031

Hewitt, C., Gilbody, S., Brealey, S., Paulden, S., Mann, R., Green, J., Morrell, J., Barkham, M., Light, K., & Richards, D. (2009). Methods to identify postnatal depression in primary care: An integrated evidence synthesis and value of information analysis. *Health Technology Assessment, 13*(36), 147-230. https://doi.org/10.3310/hta13360

Hoyer, J., Wieder, G., Höfler, M., Krause, L., Wittchen, H.U., & Martini, J. (2020). Do lifetime

anxiety disorders (anxiety liability) and pregnancy-related anxiety predict complications during pregnancy and delivery? *Early Human Development, 144*, 105022. https://doi.org/10.1016/j.earlhumdev.2020.105022

Inness, B.E., Furtado, M., Barrett, E., Stallwood, E., Streiner, D.L., McCabe, R.E., & Green, S.M. (2023). Psychometric properties of the PSWQ in a sample of pregnant and postpartum women. *Journal of Reproductive and Infant Psychology,* 1-16. https://doi.org/10.1080/02646838.2023.2209101

Irwin, J.L., Poggi Davis, E., Hobel, C.J., Coussons-Read, M., & Dunkel Schetter, C. (2020). Maternal prenatal anxiety trajectories and infant developmental outcomes in one-year-old offspring. *Infant Behavior and Development, 60*, 101468. https://doi.org/10.1016/j.infbeh.2020.101468

Johnson, S.U., Ulvenes, P.G., Øktedalen, T., & Hoffart, A. (2019). Psychometric properties of the General Anxiety Disorder 7-Item (GAD-7) Scale in a heterogenous psychiatric sample. *Frontiers in Psychology, 10*, 1713. https://doi.org/10.3389/fpsyg.2019.01713

Kaçar-Başaran, S., & Gökdağ, C. (2025). From self-compassion to obsessive-compulsive symptoms: The mediator role of intolerance of uncertainty. *Current Psychology, 44*, 2375-2384. https://doi.org/10.1007/s12144-025-07324-x

Kernot, J., Olds, T., Lewis, L.K., & Maher, C. (2015). Test-retest reliability of the English version of the Edinburgh Postnatal Depression Scale. *Archives of Women's Mental Health, 18*(2), 255-257. https://doi.org/10.1007/s00737-014-0461-4

Larsen, D.L., Attkisson, C.C., Hargreaves, W.A., & Nguyen, T.D. (1979). Assessment of client/patient satisfaction: Development of a general scale. *Evaluation and Program Planning, 2*(3), 197-207. https://doi.org/10.1016/0149-0149-7189(79)90094-6

Le Bas, G.A., Youssef, G.J., Macdonald, J.A., Rossen, L., Teague, S.J., Kothe, E.J., McIntosh, J.E., Olsson, C.A., & Hutchinson, D.M. (2022). The role of antenatal and postnatal maternal bonding in infant development. *Journal of the American Academy of Child and Adolescent Psychiatry, 61*(6), 820-829. https://doi.org/10.1016/j.jaac.2021.08.024

Levis, B., Negeri, Z., Sun, Y., Benedetti, A., Thombs, B.D., & DEPRESSion Screening Data (DEPRESSD) EPDS Group. (2020). Accuracy of the Edinburgh Postnatal Depression Scale (EPDS) for screening to detect major depression among pregnant and postpartum women: Systematic review and meta-analysis of individual participant data. *BMJ, 11*, 371. https://doi.org/10.1136/bmj.m4022

Mahoney, A.E.J., & McEvoy, P.M. (2012). A transdiagnostic examination of intolerance of uncertainty across anxiety and depressive disorders. *Cognitive Behaviour Therapy, 41*(3), 212-222. https://doi.org/10.1080/16506073.2011.622130

Marcotte-Beaumier, G., Bouchard, S., Gosselin, P., Langlois, F., Belleville, G., Marchand, A., & Dugas, M.J. (2021). The role of intolerance of uncertainty and working alliance in the outcome of cognitive behavioral therapy for generalized anxiety disorder delivery by videoconference: Mediation analysis. *JMIR Mental Health, 8*(3), e24541. https://doi.org/10.2196/24541

Meyer, T.J., Miller, M.L., Metzger, R.L., & Borkovec, T.D. (1990). Development and validation of the Penn State Worry Questionnaire. *Behaviour Research and Therapy, 28*(6), 487-495. https://doi.org/10.1016/0005-7967(90)90135-6

Miller, M.L., & McGuire, J.F. (2023). Targeting intolerance of uncertainty in treatment: A meta-analysis of therapeutic effects, treatment moderators, and underlying mechanisms. *Journal of Affective Disorders, 341*, 283-295. https://doi.org/10.1016/j.jad.2023.08.132

Morales-Munoz, I., Ashdown-Doel, B., Beazley, E., Carr, C., Preece, C., & Marwaha, S. (2023). Maternal postnatal depression and anxiety and the risk for mental health disorders in adolescent offspring: Findings from the Avon Longitudinal Study of Parents and Children cohort. *Australian and New Zealand Journal of Psychiatry, 57*(1), 82-92. https://doi.org/10.1177/000448674221082519

Morriss, J., Rodriguez-Sobstel, C., & Steinman, S.A. (2024). Intolerance of uncertainty is associated with heightened arousal during extinction learning and retention: Preliminary evidence from a clinical sample with anxiety and obsessive-compulsive disorders. *Cognitive Therapy and Research, 48*, 854-865. https://doi.org/10.1007/s10608-024-10491-z

O'Dea, G., Youssef, G.J., Hagg, L.J., Francis, L.M., Spry, E.A., Rossen, L., Smith, I., Teague, S.J., Mansour, K., Booth, A., Davies, S., Hutchinson, D., & Macdonald, J.A. (2023). Associations between maternal psychological distress and mother-infant bonding: A systematic review and meta-analysis. *Archives of Womens Mental Health, 26*(4), 441-452. https://doi.org/10.1007/s00737-023-01332-1

Pentecost, R., Latendresse, G., & Smid, M. (2021). Scoping review of the associations between perinatal substance use and perinatal depression and anxiety. *Journal of Obstetric, Gynecologic & Neonatal Nursing, 50*(4), 382-391. https://doi.org/10.1016/j.jogn.2021.02.008

Robichaud, M. (2013). Cognitive behavior therapy targeting intolerance of uncertainty: Application to a clinical case of generalized anxiety disorder. *Cognitive and Behavioral Practice. 20*(3), 251-263. https://doi.org/10.1016/j.cbpra.2012.09.001

Roddy Mitchell, A., Gordon, H., Atkinson, J., Lindquist, A., Walker, S.P., Middleton, A., Tong,

S., & Hastie, R. (2023). Prevalence of perinatal anxiety and related disorders in low- and middle-income countries: A systematic review and meta-analysis. *JAMA Network Open, 6*(11), e2343711. https://doi.org/10.1001/jamanetworkopen.2023.43711

Rodriguez-Biglieri, R., & Vetere, G.L. (2011). Psychometric characteristics of the Penn State Worry Questionnaire in an Argentinean sample: A cross-cultural contribution. *The Spanish Journal of Psychology, 14*(1), 452-463. https://doi.org/10.5209/rev_sjop.2011.v14.n1.41

Rogers, A., Obst, S., Teague, S.J., Rossen, L., Spry, E.A., Macdonald, J.A., Sunderland, M., Olsson, C.A., Youssef, G., & Hutchinson, D. (2020). Association between maternal perinatal depression and anxiety and child and adolescent development. *JAMA Pediatrics, 174*(11), 1-11. https://doi.org/10.1001/jamapediatrics.2020.2910

Sahib, A., Chen, J., Cárdenas, D., & Calear, A.L. (2023). Intolerance of uncertainty and emotion regulation: A meta-analytic and systematic review. *Clinical Psychology Review, 101*, 102270. https://doi.org/10.1016/j.cpr.2023.102270

Schwarze, C.E., von der Heiden, S., Wallwiener, S., & Pauen, S. (2024). The role of perinatal maternal symptoms of depression, anxiety and pregnancy-specific anxiety for infant's self-regulation: A prospective longitudinal study. *Journal of Affective Disorders, 346*, 144-153. https://doi.org/10.1016/j.jad.2023.10.035

Shear, M.K., Vander Bilt, J., Rucci, P., Endicott, J., Lydiard, B., Otto, M.W., Pollack, M.H., Chandler, L., Williams, J., Ali, A., & Frank, D.M. (2001). Reliability and validity of a structured interview guide for the Hamilton Anxiety Rating Scale (SIGH-A). *Depression and Anxiety, 13*(4), 166-178. https://doi.org/10.1002/da/1033

Simpson, W., Glazer, M., Michalski, N., Steiner, M., & Frey, B.N. (2014). Comparative efficacy

of the Generalized Anxiety Disorder 7-Item Scale and the Edinburgh Postnatal Depression Scale as screening tools for generalized anxiety disorder in pregnancy and the postpartum period. *Canadian Journal of Psychiatry, 59*(8), 434-440. https://doi.org/10.1177/070674371405900806

Sloan, E., Hall, K., Moulding, R., Bryce, S., & Mildred, H. (2017). Emotion regulation as a transdiagnostic treatment construct across anxiety, depression, substance, eating and borderline personality disorders: A systematic review. *Clinical Psychology Review, 57*, 141-163. https://doi.org/10.1016/j.cpr.2017.09.002

Smith, M.V., Shao, L., Howell, H., Wang, H., Poschman, K., & Yonkers, K.A. (2009). Success of mental health referral among pregnant and postpartum women with psychiatric distress. *General Hospital Psychiatry, 31*(2), 155-162. https://doi.org/10.1016/j.genhosppsych.2008.10.002

Spitzer, R.L., Kroenke, K., Williams, J.B., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: The GAD-7. *Archives of Internal Medicine, 166*(10), 1092-1097. https://doi.org/10.1001/archinte.166.10.1092

Spry, E.A., Aarsman, S.R., Youssef, G.J., Patton, G.C., Macdonald, J.A., Sanson, A., Thomson, K., Hutchinson, D.M., Letcher, P., & Olsson, C.A. (2020). Maternal and paternal depression and anxiety and offspring infant negative affectivity: A systematic review and meta-analysis. *Developmental Review, 58*, 100934. https://doi.org/10.1016/j.dr.2020.100934

Stevenson, K., Fellmeth, G., Edwards, S., Calver, C., Bennett, P., Campbell, O.M.R., & Fuhr,

D.C (2023). The global burden of perinatal common mental health and substance use among migrant women: a systematic review and meta-analysis. *The Lancet Public Health, 8*(3), e203-e216. https://doi.org/10.1016/S2468-2667(22)00342-5

Thomas, N., Komiti, A., & Judd, F. (2014). Pilot early intervention antenatal group program for pregnant women with anxiety and depression. *Archives of Women's Mental health*, *17*(6), 503–509. https://doi.org/10.1007/s00737-014-0447-2

Toscano, M., Royzer, R., Castillo, D., Li, D., & Poleshuck, E. (2021). Prevalence of depression or anxiety during antepartum hospitalization for obstetric complications: A systematic review and meta-analysis. *Obstetrics & Gynecology, 137*(5), 881-891. https://doi.org/10.1097/AOG0000000000004335

Vagos, P., Mateus, V., Silva, J., Araújo, V., Xavier, A., & Palmeira, L. (2023). Mother-infant bonding in the first nine months postpartum: The role of mother's attachment style and psychological flexibility. *Journal of Reproductive and Infant Psychology, 43*(2), 472-486. https://doi.org/10.1080/02646838.2023.2242379

van der Heiden, C., Muris, P., & van der Molen, H.T. (2012). Randomized controlled trial on the effectiveness of metacognitive therapy and intolerance-of-uncertainty therapy for generalized anxiety disorder. *Behaviour Research and Therapy, 50*(2), 100-109. https://doi.org/10.1016/j.brat.2011.12.005

Villarreal-Zegarra, D., Paredes-Angeles, R., Mayo-Puchoc, N., Arenas-Minaya, E., Huarcaya-Victoria, J., & Copez-Lonzoy, A. (2024). Psychometric properties of the GAD-7 (General Anxiety Disorder-7): A cross-sectional study of the Peruvian general population. *BMC Psychology, 12*(183). https://doi.org/10.1186-s40359-024-01688-8

Vismara, L., Sechi, C., Neri, M., Paoletti, A., & Lucarelli, L. (2020). Maternal perinatal

depression, anxiety, fear of birth, and perception of infants' negative affectivity at three months. *Journal of Reproductive and Infant Psychology, 39*(5), 532-543. https://doi.org/10.1080/02646838.2020.1843612

Voegtline, K., Payne, J.L., Standeven, L.R., Sundel, B., Pangtey, M., & Osborne, L.M. (2021). Using the Penn State Worry Questionnaire in the peripartum. *Journal of Women's Health, 30*(12), 1761-1768. https://doi.org/10.1089/jwh.2020.8669

Wagner Moyer, S., Ameringer, S., Elswick Jr., R.K., Nunziato, J.D., & Kinser, P.A. (2024). Exploration of the psychometric properties of the EPDS-US, a validation study. *Journal of Affective Disorders, 352,* 193-198. https://doi.org/10.1016/j.jad.2024.02.025

Weathers, F.W., Litz, B.T., Keane, T.M., Palmieri, P.A., Marx, B.P., & Schnurr, P.P. (2013). The PTSD Checklist for DSM-5 (PCL-5). Scale available from the National Center for PTSD at www.ptsd.va.gov

Weis, K.L., Walker, K.C., Chan, W., Yuan, T.T., & Lederman, R.P. (2020). Risk of preterm birth and newborn low birthweight in military women with increased pregnancy-specific anxiety. *Military Medicine, 185*(5-6), e678-e685. https://doi.org/10.1093/milmed/usz399

Wilson, E.J., Abbott, M.J., & Norton, A.R. (2023). The impact of psychological treatment on intolerance of uncertainty in generalized anxiety disorder: A systematic review and meta-analysis. *Journal of Anxiety Disorders, 97,* 102729. https://doi.org/10.1016/j/janxdis.2023.102729

Womersley, K., & Alderson, H. (2024). Perinatal mental health. *Medicine, 52*(10), 632-636. https://doi.org/10.1016/j.mpmed.2024.07.009

Zemestani, M., Beheshti, N., Rezaei, F., van der Heiden, C., & Kendall, P. C. (2021). Cognitive

behavior therapy targeting intolerance of uncertainty versus selective serotonin reuptake inhibitor for generalized anxiety disorder: A randomized clinical trial. *Behaviour Change, 38*(4), 250–262. https://doi.org/10.1017/bec.2021.16

Chapter 5: General Discussion

5.1 Summary of Findings

The perinatal period is marked by profound change and uncertainty and is a well-known period of increased psychological vulnerability (Anderson et al., 2017; Awini et al., 2023; Giardinelli et al., 2012; Munk-Olsen & Agerbo, 2015; Womersley & Alderson, 2024). Anxiety disorders are now recognized as the most prevalent mental health condition during the perinatal period, with prevalence rates estimated to be between 15% and 25% (Dennis et al., 2017; Fawcett et al., 2019; Roddy Mitchell et al., 2023). Although anxiety disorders during the perinatal period are associated with a wide range of adverse outcomes, research in the *prevention* of anxiety disorders remains notably limited. In contrast to the more extensive literature on the prevention of postpartum depression, research focused on preventing anxiety disorders during the perinatal period based on known risk factors remains limited, highlighting a significant gap in the field.

Among the risk factors identified in perinatal anxiety research, IU stands out as a modifiable risk factor that is also an important mechanism in anxiety disorders in general populations (e.g., Bomyea et al., 2015; Ladouceur et al., 2000; Meeten et al., 2012). Little is known however, as to whether targeting a modifiable risk factor such as IU during pregnancy can prevent the onset of anxiety disorders in the postpartum period. This program of research sought to: (1) validate a clinically meaningful self-report measure assessing IU to improve detection of anxiety disorders during the perinatal period and identify individuals who may be at increased risk of such disorders; (2) develop a CBT protocol targeting IU during pregnancy for individuals identified as *high risk* based on IU levels; and (3) evaluate the effectiveness of this CBT for IU protocol in preventing the onset of anxiety disorders during the postpartum period.

5.1.1 Study One

Given previous research identifying IU as a risk factor for anxiety worsening in the postpartum period (Furtado et al., 2019), study one sought to validate a widely used and clinically meaningful measure, the 27-item IUS (Buhr & Dugas, 2002; Freeston et al., 1994), in a perinatal sample. Specifically, we examined the psychometric properties of the IUS in a perinatal population. We also aimed to identify a clinically meaningful cut-off score on the IUS that could be used to improve detection of anxiety disorders in perinatal individuals.

Our analyses supported the use of the IUS as a screening tool for anxiety disorders during the perinatal period, demonstrating strong psychometric properties. The IUS demonstrated excellent internal consistency and good test-retest reliability, and we found evidence of both convergent validity with commonly used measures of anxiety, worry, and emotion regulation, and discriminant validity with a depression measure. Lastly, this study identified an optimal clinical cut-off score of 64 or greater on the IUS, which demonstrated excellent accuracy in detecting anxiety disorders during the perinatal period. While the role of IU in anxiety disorders has been well-established in the general population (e.g., Carleton, 2012; Counsell et al., 2017; Dugas & Robichaud, 2007; Morriss et al., 2023) and more recently recognized as a risk factor for anxiety worsening in the postpartum period (Furtado et al., 2019), this was the first study to specifically evaluate the IUS as a screening tool for anxiety in perinatal individuals. This study adds to the limited research on validated screening tools for anxiety during the perinatal period by demonstrating the clinical utility of the IUS.

5.1.2 Study Two

Study two was a study protocol outlining a proof-of-concept randomized controlled trial designed to evaluate a novel CBT protocol targeting IU during pregnancy. As part of this study,

we developed a brief, six-session, individual CBT for IU protocol, including complete therapist and participant workbooks to guide delivery. The session content was developed based on previous CBT for IU protocols used in non-perinatal populations (Dugas et al., 2022; Hebert & Dugas, 2019; Robichaud, 2013; van der Heiden et al., 2012), as well as a CBT for perinatal anxiety protocol for perinatal specific psychoeducation (Green et al., 2018).

Study two was built upon our findings from study one, which supported the use of the IUS as a valid screening tool. We were specifically interested in determining whether we could identify perinatal individuals who met the optimal clinical cut-off score on the IUS (64 or greater) but did not currently meet diagnostic criteria for an anxiety disorder. These individuals would be classified as *high risk* based on their elevated IU, a known risk factor for postpartum anxiety worsening (Furtado et al., 2019). This study focused on developing the detailed study methodology and procedures, along with the session-by-session CBT for IU content, prior to evaluating its effectiveness in preventing anxiety disorder onset during the postpartum among *high risk* pregnant individuals in study three.

5.1.3 Study Three

Study three involved conducting the proof-of-concept randomized controlled trial designed to evaluate the effectiveness of the CBT for IU protocol in preventing the onset of anxiety disorders in the postpartum period. We were interested in determining whether CBT for IU could reduce the risk of anxiety disorder onset in the postpartum period, compared to care as usual. Specifically, we examined: (1) the proportion of perinatal individuals in each group (CBT-IU and CAU) who met diagnostic (or provisional) criteria for an anxiety and/or related disorder in the postpartum period; (2) changes in IU over time between CBT-IU and CAU; and (3) changes in anxiety, worry, and depression symptoms, as well as emotion regulation.

Results from this study provide strong preliminary support for the effectiveness of a CBT-IU protocol in preventing the onset of anxiety disorders in the postpartum period. Notably, none of the participants in the CBT-IU group met diagnostic criteria for an anxiety and/or related disorder postpartum, compared to 31.6% in the CAU group. Further, the CBT-IU group exhibited significantly greater reductions in IU, worry, and anxiety, as well as significant improvements in emotion regulation.

This study aligns with prevention strategies established in the perinatal depression field, where identifying individuals at increased risk of postpartum depression, based on known risk factors, and providing psychological interventions, such as CBT, have been shown to prevent the onset of postpartum depression (Force USPST et al., 2019; O'Connor et al., 2019; Vigod et al., 2025). Similarly, our findings suggest that delivering a brief CBT protocol to individuals identified as *high risk* based on elevated IU, a risk factor for anxiety worsening in the postpartum, can significantly reduce the risk of anxiety disorder onset during the postpartum period.

The results of this study highlight the potential of a preventative strategy targeting IU, a well-recognized psychological risk factor, as an effective approach to reducing the onset of anxiety disorders in the postpartum in individuals with increased vulnerability during pregnancy. If these findings are replicated in a larger randomized controlled trial, they would support the broader implementation of a preventative strategy for perinatal individuals identified as *high risk* for anxiety disorders in the postpartum based on elevated IU across perinatal mental health services. This study is a major step forward in addressing a significant gap in anxiety disorder prevention research during the perinatal period by providing robust proof-of-concept evidence for a targeted, risk-based prevention strategy.

5.2 Significance

Together, these studies help us to better understand the role of IU in the perinatal period, both in improving symptom detection, as well as a target for preventing anxiety disorders in the postpartum period. Building on prior research identifying IU as a risk factor for anxiety worsening in the postpartum (Furtado et al., 2019), we further examined the role of IU in the perinatal period by validating a widely used measure of IU. An optimal clinical cut-off score was identified with strong psychometric properties and diagnostic accuracy for detecting anxiety disorders during this time. This research contributes to the limited literature on psychometrically sound screening tools for anxiety during the perinatal period and provides clinicians with a validated measure to help identify individuals at risk of anxiety disorders during the perinatal period. More broadly, this research addresses a critical gap in the field of perinatal mental health care, specifically in the detection of anxiety disorders during the perinatal period. Despite their high prevalence and adverse outcomes, anxiety disorders during the perinatal period are often overlooked in clinical settings, where screening efforts have historically focused on postpartum depression. One contributing factor may be the tendency to normalize heightened anxiety during the perinatal period, as it is commonly viewed as an expected response to the inherent uncertainties of pregnancy and the postpartum. These uncertainties may include not knowing how childbirth will unfold, whether the baby will be healthy, how one's sense of identity and relationships may change, and how well one will adapt to the physical and emotional demands of parenthood. While some degree of anxiety and worry are indeed common and adaptive, this over-normalization can obscure clinically significant anxiety symptoms, delay detection, and ultimately lead to poorer outcomes. Given that IU is a well-established risk factor for anxiety disorders and more recently associated with anxiety worsening in the postpartum, our validation

of the IUS provides a practical and evidence-based tool to enhance screening during the perinatal period. This research also helps bridge the gap between theory and practice by providing clinicians with a reliable, validated tool that assesses a central mechanism underlying anxiety. Its brief 27-item format, which can be completed in under five minutes, makes it a practical and efficient measure for enhancing symptom detection. This is particularly valuable in healthcare settings where time and resources for more comprehensive screening and assessment throughout the perinatal period are limited and often not feasible, such as during routine perinatal appointments in primary care, midwifery, or obstetric clinics.

Having established a method to identify individuals at increased risk of anxiety disorders during the perinatal period, this research progressed by developing and evaluating a targeted, preventative strategy. Our findings provide initial support for the effectiveness of a brief, CBT-IU protocol in preventing the onset of anxiety disorders in the postpartum among pregnant individuals who may be at increased risk. These findings also align with successful prevention efforts in the postpartum depression field, where identifying individuals based on known risk factors and providing psychological interventions has been shown to reduce the likelihood of postpartum depression onset. By targeting a recognized risk factor, this research offers a novel, risk-based strategy for preventing anxiety disorders in the postpartum period in individuals at increased risk of such disorders.

Prevention is especially important during the perinatal period, as this is already a time of increased psychological vulnerability, particularly when underlying risk factors, such as heightened IU, may be present in the absence of clinically significant anxiety symptoms. Relying solely on treatment after anxiety disorder onset can delay support and increase the risk of more severe and persistent difficulties and functional impairment. By addressing risk factors before

clinical symptoms emerge, this approach aims to reduce the incidence of anxiety disorders during the perinatal period and lessen their potential impact on functioning, well-being, and infant outcomes. While further research is needed to replicate and extend these findings, our research offers strong preliminary evidence that targeting IU through a brief, structured protocol may serve as a promising, effective preventative strategy. Ultimately, this research highlights the importance of shifting toward prevention-focused models of care that prioritize reducing risk of symptom onset before distress and impairment arise, enabling more timely and effective support that improves outcomes for perinatal individuals and their families.

5.3 Limitations and Future Directions

In addition to the limitations presented for each individual study, there are additional limitations of the larger program of research that should be considered. One limitation is the differing definition of the postpartum period across studies, specifically between study one with studies two and three. The shorter timeframe for studies two and three was selected based on the postpartum period definition noted by O'Hara and Wisner (2014) for several reasons. This timeframe was selected to support feasibility, reduce attrition in the context of a proof-of-concept trial, and capture the early onset of anxiety disorders in the postpartum period. It's also important to note that there are conflicting definitions of the postpartum period throughout the literature, ranging from four weeks postpartum (American Psychiatric Association, 2022), to three months (O'Hara & Wisner, 2014), six months (Dennis et al., 2017), and up to 12 months postpartum (O'Hara & Wisner, 2014). Given these discrepancies, future research should include longer-term follow-up extending through the first 12 months postpartum, which represents the most inclusive definition, to evaluate the long-term outcomes more comprehensively for perinatal individuals

and whether the CBT-IU protocol effectively prevents the onset of anxiety disorders across the entire postpartum period.

Another limitation to consider is the demographic homogeneity of the study samples, which primarily consisted of White, highly educated, cisgender women. The underrepresentation individuals from diverse sociodemographic backgrounds limits the extent to which our findings can be generalized. This is an important consideration given that research that has demonstrated that sociodemographic risk factors (e.g., lower education, lower SES) are associated with an increased risk for anxiety worsening during the perinatal period (Furtado et al., 2018; Leach et al., 2017). While research on IU across diverse demographic groups is limited, one recent study (Sadeh & Bounoua, 2023) found that IU may be a stronger predictor of psychiatric symptoms (not limited to anxiety) among Black adults compared to White adults. Replicating our study findings in more diverse sociodemographic populations is therefore needed to better understand the role of IU across groups and to determine whether the CBT-IU protocol is equally effective across diverse populations.

A key strength of this program of research is its focus on the perinatal population, which is significantly underrepresented in the anxiety literature when compared to the general population. Nevertheless, while IU is a well-established risk and maintenance factor for anxiety disorders in the general population (Carleton, 2012; Counsell et al., 2017; Dugas & Robichaud, 2007; Gentes & Ruscio, 2011; Gu et al., 2020; Morriss et al., 2023; Wilson et al., 2023) with the IUS being widely used, there is currently no recommended clinical cut-off score for anxiety screening outside the perinatal context. Therefore, it is unclear whether the cut-off score identified in study one would generalize to non-perinatal populations, or if different thresholds are necessary. The effectiveness of the CBT-IU protocol as a preventative strategy outside the

perinatal period also remains unknown. Future studies should determine whether an optimal cut-off score exists for the IUS in non-perinatal populations to improve anxiety symptom detection. If our findings are confirmed in a large, well-powered RCT, then the applicability and effectiveness of CBT-IU as a potential preventative strategy in the general population should be examined.

While the present program of research focused on IU, other transdiagnostic risk factors, such as anxiety sensitivity, should be considered for future research. Anxiety sensitivity refers to the tendency to fear anxiety-related sensations (e.g., heart racing, sweating) due to interpreting these sensations as harmful (Reiss, 1985). Within the perinatal population, anxiety sensitivity has been shown to be positively associated with anxiety symptoms, pregnancy-specific anxiety, and fear of childbirth (Zimmerman et al., 2025). Future research would benefit from investigating whether anxiety sensitivity can improve the detection of anxiety disorders during the perinatal period and serve as an effective prevention target, similar to IU. Enhancing our understanding of these risk factors could further improve early identification and contribute to the development of additional preventative interventions.

Finally, an important direction for future research is to examine the broader impact of the CBT-IU protocol on outcomes beyond perinatal mental health, especially given the wide range of adverse outcomes associated with anxiety disorders during the perinatal period. Future research should investigate whether targeting IU through CBT during pregnancy also leads to positive effects on an individual's self-esteem and confidence in their parenting, infant bonding, and child developmental outcomes such as temperament and emotional well-being. Exploring these areas would offer a more comprehensive understanding of the broader impact CBT-IU may have for both the perinatal individual and their child.

5.4 Conclusions

This program of research examined the role of IU during the perinatal period, making important contributions to both the detection and prevention of anxiety disorders during the perinatal period. It offers clinicians a validated, clinically meaningful measure to better identify perinatal individuals at risk of anxiety disorders during the perinatal period. In doing so, this can help facilitate early symptom detection and timely intervention, in turn reducing the adverse outcomes known to be associated with anxiety experienced during this time. The development and preliminary evaluation of a targeted CBT-IU protocol offers promising proof-of-concept evidence that addressing IU during pregnancy for individuals at increased risk, may decrease the onset of anxiety disorders during the postpartum period. These studies fill gaps in the perinatal anxiety literature, where validated screening tools and effective preventive strategies remain limited. Overall, this program of research highlights the value of proactive and prevention focused approaches during a period already characterized by heightened uncertainty and psychological vulnerability.

References: General Introduction and Discussion

American Psychiatric Association. (2022). *Diagnostic and statistical manual of mental Disorders Text Revision* (5th ed. TR). https://doi/book/10.1176/appi.books.9780890425787

Anderson, F. M., Hatch, S. L., Comacchio, C., & Howard, L. M. (2017). Prevalence and risk of mental disorders in the perinatal period among migrant women: A systematic review and meta-analysis. *Archives of Women's Mental Health*, *20*(3), 449–462. https://doi.org/10.1007/s00737-017-0723-z

Anniverno, R., Bramante, A., Mencacci, C., & Federico, D. (2013). Anxiety disorders in pregnancy and the postpartum period. In D. Federico (Ed.), *New Insights into Anxiety Disorders*. InTech.

Austin, M. V., Mule, V., Hadzi-Pavlovic, D., & Reilly, N. (2022). Screening for anxiety disorders in third trimester pregnancy: A comparison of four brief measures. *Archives of Women's Mental Health, 25*(2), 389-397. https://doi.org/10.1007/s00737-021-01166-9

Awini, E., Agyepong, I. A., Owiredu, D., Gyimah, L., Ashinyo, M. E., Yevoo, L. L., Aye, S. G. E. V., Abbas, S., Cronin De Chavez, A., Kane, S., Mirzoev, T., & Danso-Appiah, A. (2023). Burden of mental health problems among pregnant and postpartum women in sub-Saharan Africa: Systematic review and meta-analysis protocol. *BMJ Open*, *13*(6), e069545. https://doi.org/10.1136/bmjopen-2022-069545

Bauer, A., Knapp, M., & Parsonage, M. (2016). Lifetime costs of perinatal anxiety and depression. *Journal of Affective Disorders*, *192*, 83–90. https://doi.org/10.1016/j.jad.2015.12.005

Bayrampour, H., Vinturache, A., Hetherington, E., Lorenzetti, D. L., & Tough, S. (2018). Risk factors for antenatal anxiety: A systematic review of the literature. *Journal of Reproductive and Infant Psychology*, *36*(5), 476–503. https://doi.org/10.1080/02646838.2018.1492097

Bayrampour, H., Trieu, J., & Tharmaratnam, T. (2019). Effectiveness of eHealth Interventions to Reduce Perinatal Anxiety: A Systematic Review and Meta-Analysis. *The Journal of Clinical Psychiatry*, *80*(1), 18r12386. https://doi.org/10.4088/JCP.18r12386

Bergner, A., Beyer, R., Klapp, B.F., Rauchfuss, M. (2008). Pregnancy after early pregnancy loss: A prospective study of anxiety, depressive symptomatology and coping. *Journal of Psychosomatic Obstetrics & Gynecology, 29*(2)*,* 105-113. https://doi.org/10.1080/01674820701687521

Behar, E., DiMarco, I. D., Hekler, E. B., Mohlman, J., & Staples, A. M. (2009). Current theoretical models of Generalized Anxiety Disorder (GAD): Conceptual review and treatment implications. *Journal of Anxiety Disorders, 23,* 1011-1023. https://doi.org/10.1016/j.janxdis.2009.07.006

Bernstein, G. A., Layne, A. E., Egan, E. A., & Nelson, L. P. (2005). Maternal phobia anxiety and child anxiety. *Journal of Anxiety Disorders,* 19(6), 658-672. https://doi.org/10.1016/j.janxdis.2004.09.001

Biaggi, A., Conroy, S., Pawlby, S., Pariante, C.M. (2016). Identifying the women at risk of antenatal anxiety and depression: A systematic review. *Journal of Affective Disorders, 191,* 62-77. https://doi.org/10.1016/j.jad.2015.11.014

Bijsterbosch, J. M., Keizer, A., Boelen, P. A., van den Brink, F., & Sternheim, L. C. (2022). Understanding relations between intolerance of uncertainty and body checking and body

avoiding in anorexia nervosa. *Journal of Eating Disorders*, *10*(1), 122. https://doi.org/10.1186/s40337-022-00647-1

Bina, R., & Harrington, D. (2016). The Edinburgh Postnatal Depression Scale: Screening Tool for Postpartum Anxiety as Well? Findings from a Confirmatory Factor Analysis of the Hebrew Version. *Maternal and Child Health Journal*, *20*(4), 904–914. https://doi.org/10.1007/s10995-015-1879-7

Britton, J.R. (2011). Infant temperament and maternal anxiety and depressed mood in the early postpartum period. *Women & Health, 51*(1), 55-71. https://doi.org/10.1080/03630242.2011.540741

Buhr, K., & Dugas, M. J. (2006). Investigating the construct validity of intolerance of uncertainty and its unique relationship with worry. *Journal of Anxiety Disorders, 20,* 222-236. https://doi.org/10.1016/j.janxdis.2004.12.004

Buss, C., Davis, E.P., Muftuler, L.T., Head, K., Sandman, C.A. (2010). High pregnancy anxiety during mid-gestation is associated with decreased gray matter density in 6-9 year-old children. *Psychoneuroendocrinology, 35,* 141-153. https://doi.org/10.1016/j.psyneuen.2009.07.010

Buss, C., Davis, E.P., Hobel, C.J., Sandman, C.A. (2011). Maternal pregnancy-specific anxiety is associated with child executive function at 6-9 years age. *Stress, 14,* 665-676. https://doi.org/10.3109/10253890.2011.623250

Çankaya, S., & İbrahimoğlu, T. (2022). Stress, anxiety, intolerance of uncertainty, and psychological well-being characteristics of pregnant women with and without threatened miscarriage: a case-control study. *Journal of Obstetrics and Gynaecology: The Journal of*

the Institute of Obstetrics and Gynaecology, *42*(8), 3577–3583. https://doi.org/10.1080/01443615.2022.2158319

Capron, L.E., Glover, V., Pearson, R.M., Evans, J., O'Connor, T.G., Stein, A., Murphy, S. E., & Ramchandani, P.G. (2015). Associations of maternal and paternal antenatal mood with offspring anxiety disorder at age 18 years. *Journal of Affective Disorders, 187,* 20-26. https://doi.org/10.1016/j.jad.2015.08.012

Carleton, R.N. (2012). The intolerance of uncertainty construct in the context of anxiety disorders: Theoretical and practical perspectives. *Expert Review of Neurotherapeutics, 12*(8), 937-947. https://doi.org/10.1586/ern.12.82

Carleton, R.N. (2016). Into the unknown: A review and synthesis of contemporary models involving uncertainty. *Journal of Anxiety Disorders, 39*, 30-43. https://doi.org/10.1016/j.janxdis.2016.02.007

Çevik, S., & Yağmur, Y. (2018). Impact of intolerance of uncertainty on psychological well-being in pregnant women with or without miscarriage risk. *Perspectives in Psychiatric Care*, *54*(3), 436–440. https://doi.org/10.1111/ppc.12297

Chae, J., & Kim, H. K. (2021). Internet-based prenatal interventions for maternal health among pregnant women: A systematic review and meta-analysis. *Children and Youth Services Review, 127,* Article 106079. https://doi.org/10.1016/j.childyouth.2021.106079

Chin, K., Wendt, A., Bennett, I.M., & Bhat, A. (2022). Suicide and maternal mortality. *Current Psychiatry Reports, 24*(4), 239-275. https://doi.org/10.1007/s11920-022-01334-3

Ching, H., Chua, J. Y. X., Chua, J. S., & Shorey, S. (2023). The effectiveness of technology-based cognitive behavioral therapy on perinatal depression and anxiety: A systematic

review and meta-analysis. *Worldviews on Evidence-based Nursing*, *20*(5), 451–464. https://doi.org/10.1111/wvn.12673

Clinkscales, N., Golds, L., Berlouis, K., & MacBeth, A. (2023). The effectiveness of psychological interventions for anxiety in the perinatal period: A systematic review and meta-analysis. *Psychology and Psychotherapy*, *96*(2), 296–327. https://doi.org/10.1111/papt.12441

Counsell, A., Furtado, M., Iorio, C., Anand, L., Canzonieri, A., Fine, A., Fotinos, K., Epstein, I., & Katzman, M.A. (2017). Intolerance of uncertainty, social anxiety, and generalized anxiety: Differences by diagnosis and symptoms. *Psychiatry Research, 252*, 63-69. https://doi.org/10.1016/j.psychres.2017.02.046

Cox, J.L., Holden, J.M., & Sagovsky, R. (1987). Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry, 150,* 782-786. https://doi.org/10.1192/bjp.150.6.782

Davies, S.M., Silverio, S.A., Christiansen, P., & Fallon, V. (2021). Maternal-infant bonding and perceptions of infant temperament: The mediating role of maternal mental health. *Journal of Affective Disorders, 282*, 1323-1329. https://doi.org/10.1016/j.jad.2021.01.023

Davis, E.P., & Sandman, C.A. (2012). Prenatal psychobiological predictors of anxiety risk in preadolescent children. *Psychoneuroendocrinology, 37*(8)*,* 1224-1233. https://doi.org/10.1016/j.psyneuen.2011.12.016

Dennis, C.-L., Falah-Hassani, K., & Shiri, R. (2017). Prevalence of antenatal and postnatal anxiety: Systematic review and meta-analysis. *British Journal of Psychiatry*, *210*(5), 315–323. https://doi.org/10.1192/bjp.bp.116.187179

Donegan, E., Frey, B. N., McCabe, R. E., Streiner, D. L., & Green, S. M. (2022). Intolerance of Uncertainty and Perfectionistic Beliefs About Parenting as Cognitive Mechanisms of Symptom Change During Cognitive Behavior Therapy for Perinatal Anxiety. *Behavior Therapy*, *53*(4), 738–750. https://doi.org/10.1016/j.beth.2022.02.005

Dowse, E., Chan, S., Ebert, L., Wynne, O., Thomas, S., Jones, D., Fealy, S., Evans, T.E., & Oldmeadow, C. (2020). Impact of perinatal depression and anxiety on birth outcomes: A retrospective data analysis. *Maternal and Child Health Journal, 24*, 718-726. https://doi.org/10.1007/s10995-020-02906-6

Dugas, M. J., Buhr, K., & Ladouceur, R. (2004). The role of intolerance of uncertainty in etiology and maintenance. In: R. G. Heimberg, C. L. Turk, & D. S. Mennin (Eds.), Generalized anxiety disorder: advances in research and practice (pp. 143-163). New York: Guilford.

Dugas, M. J., Freeston, M. H., & Ladouceur, R. (1997). Intolerance of uncertainty and problem orientation in worry. *Cognitive Therapy and Research, 21,* 595-606. https://doi.org/10.1023/A:1021890322153

Dugas, M. J., Gagnon, F., Landouceur, R., & Freeston, M. H. (1998). Generalized anxiety disorder: A preliminary test of a conceptual model. *Behaviour Research and Therapy*, *36*, 215-226. https://doi.org/10.1016/s0005 - 7967(97)00070 - 3

Dugas, M. J., & Ladouceur, R. (2000). Treatment of GAD. Targeting intolerance of uncertainty in two types of worry. *Behavior Modification*, *24*(5), 635–657. https://doi.org/10.1177/0145445500245002

Dugas, M. J., Letarte, H., Rheaume, J., Freeston, M. H., & Ladouceur, R. (1995). Worry and problem solving: evidence of a specific relationship. *Cognitive Therapy and Research, 19,* 109-120. https://doi.org/10.1007/BF02229679

Dugas, M. J., & Robichaud, M. (2007). Cognitive-Behavioral Treatment for Generalized Anxiety Disorder: From Science to Practice. New York: Routledge.

Dunkel Schetter, C., Niles, A.N., Guardino, C.M., Khaled, M., Kramer, M.S. (2016). Demographic, medical, and psychosocial predictors of pregnancy anxiety. *Paediatric and Perinatal Epidemiology, 30(5),* 421-429. https://doi.org/10.1111/ppre.12300

Evans, K., Rennick-Egglestone, S., Cox, S., Kuipers, Y., & Spiby, H. (2022). Remotely Delivered Interventions to Support Women with Symptoms of Anxiety in Pregnancy: Mixed Methods Systematic Review and Meta-analysis. *Journal of Medical Internet Research*, *24*(2), e28093. https://doi.org/10.2196/28093

Fairbrother, N., Corbyn, N., Thordarson, D. S., Ma, A., & Surm, D. (2019). Screening for perinatal anxiety disorders: Room to grow. *Journal of Affective Disorders, 250,* 363-370. https://doi.org/10.1016/j.jad.2019.03.052

Faisal-Cury, A., & Rossi Menezes, P. (2007). Prevalence of anxiety and depression during pregnancy in private setting sample. *Archives of Women's Mental Health, 10*(1)*,* 25-32. https://doi.org/10.1007/s00737-006-0164-6

Faisal-Cury, A., Menezes, P., Araya, R., & Zugaib, M. (2009). Common mental disorders during pregnancy: prevalence and associated factors among low-income women in São Paulo, Brazil. *Archives of Women's Mental Health, 12*(5), 335-343. https://doi.org/10.1007/s00737-009-0081-6

Fawcett, E. J., Fairbrother, N., Cox, M. L., White, I. R., & Fawcett, J. M. (2019). The prevalence of anxiety disorders during pregnancy and the postpartum period: A multivariate Bayesian meta-analysis. *Journal of Clinical Psychiatry, 80*(4), 18r12527. https://doi.org/10.4088/JCP.18r12527

Flink, I.K., Engström, J., Vastamäki, S., Vixner, L., & Engman, L. (2023). Expecting the uncertain: The applicability of the intolerance of uncertainty model on fear of childbirth. *Journal of Psychosomatic Obstetrics & Gynecology, 44*(1). https://doi.org/10.1080/0167482X.2023.2243648

Freeston, M. H., Rhéaume, J., Letarte, H., Dugas, M. J., & Ladouceur, R. (1994). Why do people worry? *Personality and Individual Differences, 17,* 791-802. https://doi.org/10.1016/0191- 8869(94)90048-5

Furtado, M., Van Lieshout, R.J., Van Ameringen, M.V., Green, S.M., & Frey, B.N. (2019). Biological and psychosocial predictors of anxiety worsening in the postpartum period: A longitudinal study. *Journal of Affective Disorders, 250*(2019), 218-225. https://doi.org/10.1016/j.jad.2019.02.064

Gentes, E. L., & Ruscio, A. M. (2011). A meta-analysis of the relation of intolerance of uncertainty to symptoms of generalized anxiety disorder, major depressive disorder, and obsessive-compulsive disorder. *Clinical Psychology Review, 31*(6), 923-933. https://doi.org/10.1016/j.cpr.2011.05.001

Giardinelli, L., Innocenti, A., Benni, L., Stefanini, M. C., Lino, G., Lunardi, C., & Faravelli, C. (2012). Depression and anxiety in perinatal period: Prevalence of risk factors in an Italian sample. *Archives of Women's Mental Health, 15*(1), 21-30. https://doi.org.10.1007/s00737-011-0249-8

Giurgescu, C., Penckofer, S., Maurer, M. C., & Bryant, F. B. (2006). Impact of uncertainty, social support, and prenatal coping on the psychological well-being of high-risk pregnant women. *Nursing Research*, *55*(5), 356–365. https://doi.org/10.1097/00006199-200609000-00008

Göbel, A., Yao Stuhrmann, L., Harder, S., Schulte-Markwort, M., & Mudra, S. (2018). The association between maternal-fetal bonding and prenatal anxiety: An explanatory analysis and systematic review. *Journal of Affective Disorders, 239*, 313-327. https://doi.org/10.1016/j.jad.2018.07.024

Goldman, N., Dugas, M. J., Sexton, K. A., & Gervais, N. J. (2007). The impact of written exposure on worry: a preliminary investigation. *Behavior Modification*, *31*(4), 512–538. https://doi.org/10.1177/0145445506298651

Gong, X., Hao, J., Tao, F., Zhang, J., Wang, H., Xu, R. (2013). Pregnancy loss and anxiety and depression during subsequent pregnancies: Data from the C-ABC study. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 166*(1)*,* 30-36. https://doi.org/10.1016/j.ejogrb.2012.09.024

Green, S.M., Frey, B.N., Donegan, E., & McCabe, R.E. (2018). *Cognitive behavioural therapy for anxiety and depression during pregnancy and beyond: How to manage symptoms and maximize well-being.* Routledge.

Gu, Y., Gu, S., Lei, Y., & Li, H. (2020). From uncertainty to anxiety: How uncertainty fuels anxiety in a process mediated by intolerance of uncertainty. *Neural Plasticity, 2020*, 8866386. https://doi.org/10.115/2020/8866386

Han, L., Bai, H., Lun, B., Li, Y., Wang, Y., & Ni, Q. The prevalence of fear of childbirth and its association with intolerance of uncertainty and coping styles among pregnant Chinese

women during the COVID-19 pandemic. *Frontiers in Psychiatry, 13*, 935760. https://doi.org/10.3389/fpsyt.2022.935760

Hebert, E. A., & Dugas, M. J. (2019). Behavioral experiments for intolerance of uncertainty: Challenging the unknown in the treatment of generalized anxiety disorder. *Cognitive and Behavioral Practice, 26*(2), 421-436. https://doi.org/10.1016/j.cbpra.2018.07.007

Hennessey, E.M.P., Swales, D.A., Markant, K., Hoffman, M.C., Hankin, B.L., & Poggi Davis, E. (2023). Maternal anxiety during pregnancy predicts infant attention to affective faces. *Journal of Affective Disorders, 344*, 104-114. https://doi.org/10.1016/j.jad.2023.09.031

Howard, L. M., Oram, S., Galley, H., Trevillion, K., & Feder, G. (2013). Domestic violence and perinatal mental disorders: a systematic review and meta-analysis. *PLoS medicine*, *10*(5), e1001452. https://doi.org/10.1371/journal.pmed.1001452

Hoyer, J., Wieder, G., Höfler, M., Krause, L., Wittchen, H.U., & Martini, J. (2020). Do lifetime anxiety disorders (anxiety liability) and pregnancy-related anxiety predict complications during pregnancy and delivery? *Early Human Development, 144*, 105022. https://doi.org/10.1016/j.earlhumdev.2020.105022

Irwin, J.L., Poggi Davis, E., Hobel, C.J., Coussons-Read, M., & Dunkel Schetter, C. (2020). Maternal prenatal anxiety trajectories and infant developmental outcomes in one-year-old offspring. *Infant Behavior and Development, 60*, 101468. https://doi.org/10.1016/j.infbeh.2020.101468

Jacoby, R. J., & Abramowitz, J. S. (2017). Intolerance of uncertainty in OCD. In C. Pittenger (Ed.), *Obsessive-compulsive disorder: Phenomenology, pathophysiology, and treatment* (pp. 171–177). Oxford University Press.

Jomeen, J., & Martin, C. R. (2005). Confirmation of an occluded anxiety component within the Edinburgh Postnatal Depression Scale (EPDS) during early pregnancy. *Journal of Reproductive and Infant Psychology, 23*(2), 143–154. https://doi.org/10.1080/02646830500129297

Kaçar-Başaran, S., & Gökdağ, C. (2025). From self-compassion to obsessive-compulsive symptoms: The mediator role of intolerance of uncertainty. *Current Psychology, 44*, 2375-2384. https://doi.org/10.1007/s12144-025-07324-x

Karaçam, Z., & Ançel, G. (2009). Depression, anxiety and influencing factors in pregnancy: a study in a Turkish population. *Midwifery*, *25*(4), 344–356. https://doi.org/10.1016/j.midw.2007.03.006

Kesby, A., Maguire, S., Vartanian, L. R., & Grisham, J. R. (2019). Intolerance of uncertainty and eating disorder behaviour: Piloting a consumption task in a non-clinical sample. *Journal of Behavior Therapy and Experimental Psychiatry*, *65*, 101492. https://doi.org/10.1016/j.jbtep.2019.101492

Knowles, K. A., & Olatunji, B. O. (2023). Intolerance of uncertainty as a cognitive vulnerability for obsessive-compulsive disorder: A qualitative review. *Clinical Psychology, 30*(3), 317-330. https://doi.org/10.1037/cps0000150

Koerner, N., & Dugas, M. J. (2006). A cognitive model of generalized anxiety disorder: The role of intolerance of uncertainty. In G. C. L. Davey & A. Wells (Eds.), Worry and Its Psychological Disorders: Theory, Assessment and Treatment (pp. 201-216). Chichester: Wiley.

Koukopoulos, A., Mazza, C., De Chiara, L., Sani, G., Simonetti, A., Kotzalids, G. D., Armani, G., Callovini, G., Bonito, M., Parmigiani, G., Ferracuti, S., Somerville, S., Roma, P., &

Angeletti, G. (2021). Psychometric properties of the Perinatal Anxiety Screening Scale administered to Italian women in the perinatal period. *Frontiers in Psychiatry, 12,* 684579. https://doi.org/10.3389/fpsyt.2021.684579

Ladouceur, R., Gosselin, P., & Dugas, M. J. (2000). Experimental manipulation of intolerance of uncertainty: A study of a theoretical model of worry. *Behaviour Research and Therapy, 38*(9), 933–941. https://doi.org/10.1016/S0005-7967(99)00133-3

Le Bas, G.A., Youssef, G.J., Macdonald, J.A., Rossen, L., Teague, S.J., Kothe, E.J., McIntosh, J.E., Olsson, C.A., & Hutchinson, D.M. (2022). The role of antenatal and postnatal maternal bonding in infant development. *Journal of the American Academy of Child and Adolescent Psychiatry, 61*(6), 820-829. https://doi.org/10.1016/j.jaac.2021.08.024

Leach, L. S., Poyser, C., & Fairweather-schmidt, K. (2017). Maternal perinatal anxiety: A review of prevalence and correlates. *Clinical Psychologist*, *21*(1), 4–19. https://doi.org/10.1111/cp.12058

Lederman, R., & Weis, K. (2009). *Psychosocial adaptation to pregnancy: Seven Dimensions of Maternal Role Development*. Springer Science & Business Media.

Leeners, B., Richter-Appelt, H., Imthurn, B., & Rath, W. (2006). Influence of childhood sexual abuse on pregnancy, delivery, and the early postpartum period in adult women. *Journal of Psychosomatic Research*, *61*(2), 139–151. https://doi.org/10.1016/j.jpsychores.2005.11.006

Leng, L. L., Yin, X. C., & Ng, S. M. (2023). Mindfulness-based intervention for clinical and subthreshold perinatal depression and anxiety: A systematic review and meta-analysis of randomized controlled trial. *Comprehensive Psychiatry*, *122*, 152375. https://doi.org/10.1016/j.comppsych.2023.152375

Marchesi, C., Ampollini, P., Paraggio, C., Giaracuni, G., Ossola, P., De Panfilis, C., Tonna, M., & Viviani, D. (2014). Risk factors for panic disorder in pregnancy: a cohort study. *Journal of Affective Disorders*, *156*, 134–138. https://doi.org/10.1016/j.jad.2013.12.006

Marsay, C., Manderson, L., & Subramaney, U. (2017). Validation of the Whooley questions for antenatal depression and anxiety among low-income women in urban South Africa. *South African Journal of Psychiatry, 23,* 1013. https://doi.org/10.4102/sajpsychiatry.v23i0.1013

Martini, J., Petzoldt, J., Einsle, F., Beesdo-Baum, K., Höfler, M., & Wittchen, H.U. (2015). Risk factors and course patterns of anxiety and depressive disorders during pregnancy and after delivery: A prospective-longitudinal study. *Journal of Affective Disorders, 175,* 385-395. https://doi.org/j.jad.2015.01.012

Matthey, S.(2008). Using the Edinburgh Postnatal Depression Scale to screen for anxiety disorders. Depression & Anxiety, 25, 926–931. https://doi.org/10.1002/da.20415.

McEvoy, P. M., & Mahoney, A. E. (2012). To be sure, to be sure: intolerance of uncertainty mediates symptoms of various anxiety disorders and depression. *Behavior Therapy*, *43*(3), 533–545. https://doi.org/10.1016/j.beth.2011.02.007

McEvoy, P. M., & Mahoney, A. E. (2013). Intolerance of uncertainty and negative metacognitive beliefs as transdiagnostic mediators of repetitive negative thinking in a clinical sample with anxiety disorders. *Journal of Anxiety Disorders*, *27*(2), 216–224. https://doi.org/10.1016/j.janxdis.2013.01.006Mezey, G., Bacchus, L., Bewley, S., & White, S. (2005). Domestic violence, lifetime trauma and psychological health of childbearing women. *BJOG: An International Journal of Obstetrics and Gynaecology*, *112*(2), 197–204. https://doi.org/10.1111/j.1471-0528.2004.00307.x

Meeten, F., Dash, S. R., Scarlet, A. L., & Davey, G. C. (2012). Investigating the effect of intolerance of uncertainty on catastrophic worrying and mood. *Behaviour Research and Therapy*, *50*(11), 690–698. https://doi.org/10.1016/j.brat.2012.08.003

Milgrom, J., Schembri, C., Ericksen, J., Ross, J., & Gemmill, A. W. (2011). Towards parenthood: an antenatal intervention to reduce depression, anxiety and parenting difficulties. *Journal of Affective Disorders*, *130*(3), 385–394. https://doi.org/10.1016/j.jad.2010.10.045

Misri, S., Abizadeh, J., Sanders, S., & Swift, E. (2015). Perinatal generalized anxiety disorder: Assessment and treatment. *Journal of Women's Health, 24,* 762-770. https://doi.org/10.1089/jwh.2014.5150

Moore, P.S., Whaley, S.E., Sigman, M. (2004). Interactions between mothers and children: Impacts of maternal and child anxiety. *Journal of Abnormal Psychology, 113*(3)*,* 471-476. https://doi.org/10.1037/0021-843X.113.3.471

Morriss, J., Goh, K., Hirsch, C.R., & Dodd, H.F. (2023). Intolerance of uncertainty heightens negative emotional states and dampens positive emotional states. *Frontiers in Psychiatry, 14*, 1147970. https://doi.org/10.3389/fpsyt.2023.1147970

Munk-Olsen, T., & Agerbo, E. (2015). Does childbirth cause psychiatric disorders? A population-based study paralleling a natural experiment. *Epidemiology, 26,* 79–84. https://doi. org/10.1097/EDE.0000000000000193

Nasreen, H. E., Kabir, Z. N., Forsell, Y., & Edhborg, M. (2011). Prevalence and associated factors of depressive and anxiety symptoms during pregnancy: A population based study in rural Bangladesh. *BMC Women's Health*, *11*, 22. https://doi.org/10.1186/1472-6874-11-22

O'Connor, E., Senger, C. A., Henninger, M. L., Coppola, E., & Gaynes, B. N. (2019). Interventions to Prevent Perinatal Depression: Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA*, *321*(6), 588–601. https://doi.org/10.1001/jama.2018.20865

O'Dea, G., Youssef, G.J., Hagg, L.J., Francis, L.M., Spry, E.A., Rossen, L., Smith, I., Teague, S.J., Mansour, K., Booth, A., Davies, S., Hutchinson, D., & Macdonald, J.A. (2023). Associations between maternal psychological distress and mother-infant bonding: A systematic review and meta-analysis. *Archives of Women's Mental Health, 26*(4), 441-452. https://doi.org/10.1007/s00737-023-01332-1

O'Hara, M. W., & Wisner, K. L. (2014). Perinatal mental illness: Definition, description and aetiology. *Best Practice & Research Clinical Obstetrics and Gynaecology, 28,* 3-12. DOI: 10.1016/j.bpobgyn.2013.09.002

O'Mahen, H., Himle, J. A., Fedock, G., Henshaw, E., & Flynn, H. (2013). A pilot randomized controlled trial of cognitive behavioral therapy for perinatal depression adapted for women with low incomes. *Depression and Anxiety*, *30*(7), 679–687. https://doi.org/10.1002/da.22050

Orsolini, L., Valchera, A., Vecchiotti, R., Tomasetti, C., Iasevoli, F., Fornaro, M., De Berardis, D., Perna, G., Pompili, M., & Bellantuono, C. (2016). Suicide during perinatal period: Epidemiology, risk factors, and clinical correlates. *Frontiers in Psychiatry, 7*, 138. https://doi.org/10.3389/fpsyt.2016.00138

Pentecost, R., Latendresse, G., & Smid, M. (2021). Scoping review of the associations between perinatal substance use and perinatal depression and anxiety. *Journal of Obstetric,*

Gynecologic & Neonatal Nursing, 50(4), 382-391. https://doi.org/10.1016/j.jogn.2021.02.008

Peter, P. J., de Mola, C. L., de Matos, M. B., Coelho, F. M., Pinheiro, K. A., da Silva, R. A., Castelli, R. D., Pinheiro, R. T., & Quevedo, L. A. (2017). Association between perceived social support and anxiety in pregnant adolescents. *Brazilian Journal of Psychiatry*, *39*(1), 21–27. https://doi.org/10.1590/1516-4446-2015-1806

Phillips, J., Charles, M., Sharpe, L., & Matthey, S. (2009). Validation of the subscales of the Edinburgh Postnatal Depression Scale in a sample of women with unsettled infants. *Journal of Affective Disorders,* 118, 101-112. https://doi.org/10.1016/j.jad.2009.02.004

Pinciotti, C. M., Riemann, B. C., & Abramowitz, J. S. (2021). Intolerance of uncertainty and obsessive-compultsive disorder dimensions. *Journal of Anxiety Disorders, 81*, 102417. https://doi.org/10.1016/j.janxdis.2021.102417

Qiao, Y.X., Wang, J., Li, J., Ablat, A. (2009). The prevalence and related risk factors of anxiety and depression symptoms among Chinese pregnant women in Shanghai. *Australian and New Zealand Journal of Obstetrics and Gynecology, 49*(2)*,* 185-190. https://doi.org/10.1111/j.1479-828X.2009.00966.x

Qiu, C., Williams, M. A., Calderon-Margalit, R., Cripe, S. M., & Sorensen, T. K. (2009). Preeclampsia risk in relation to maternal mood and anxiety disorders diagnosed before or during early pregnancy. *American Journal of Hypertension, 22*(4), 397-402. https://doi.org/10.1038/ajh.2008.366

Rees, S., Channon, S., & Waters, C. S. (2019). The impact of maternal prenatal and postnatal anxiety on children's emotional problems: A systematic review. *European Child & Adolescent Psychiatry*, *28*(2), 257–280. https://doi.org/10.1007/s00787-018-1173-5

Robichaud, M. (2013). Cognitive behavior therapy targeting intolerance of uncertainty: Application to a clinical case of generalized anxiety disorder. *Cognitive and Behavioral Practice, 20*(3), 251–263. https://doi.org/10.1016/j.cbpra.2012.09.001

Robichaud, M., & Dugas, M. J. (2005). Negative problem orientation (Part III): Construct validity and specificity to worry. *Behaviour Research and Therapy, 43,* 403-412. https://doi.org/10.1016/j.brat.2004.02.008

Roddy Mitchell, A., Gordon, H., Atkinson, J., Lindquist, A., Walker, S. P., Middleton, A., Tong, S., & Hastie, R. (2023). Prevalence of perinatal anxiety and related disorders in low- and middle-income countries: A systematic review and meta-analysis. *JAMA Network Open, 6*(11), e2343711. https://doi.org/10.1001/jamanetworkopen.2023.43711

Rogers, A., Obst, S., Teague, S.J., Rossen, L., Spry, E.A., Macdonald, J.A., Sunderland, M., Olsson, C.A., Youssef, G., & Hutchinson, D. (2020). Association between maternal perinatal depression and anxiety and child and adolescent development: A meta-analysis. *JAMA Pediatrics, 174*(11), 1082-1092. https://doi.org/10.1001/jamapediatrics.2020.2910

Rondung, E., Ekdahl, J., & Sundin, O. (2019). Potential mechanisms in fear of birth: The role of pain catastrophizing and intolerance of uncertainty. *Birth, 46*(1), 61-68. https://doi.org/10.1111/birt.12368

Ross, L. E., & McLean, L. M. (2006). Anxiety disorders during pregnancy and the postpartum period: A systematic review. *The Journal of Clinical Psychiatry*, *67*(8), 1285–1298. https://doi.org/10.4088/jcp.v67n0818

Ross, K.M., Letourneau, N., Climie, E., Giesbrecht, G., & Dewey, D. (2020). Perinatal maternal anxiety and depressive symptoms and child executive function and attention at two-years

of age. *Developmental Neuropsychology, 45*(6), 380-395. https://doi.org/10.1080/87565641.2020.1838525

Rubertsson, C., Hellstrom, J., Cross, M., Sydsjo, G. (2014). Anxiety in early pregnancy: Prevalence and contributing factors. *Archives of Women's Mental Health, 17(3),* 221-228. https://doi.org/10.1007/s00737-013-0409-0

Sadeh, N., & Bounoua, N. (2023). Race moderates the impact of intolerance of uncertainty on mental health symptoms in Black and White community adults. *Journal of anxiety disorders*, *93*, 102657. https://doi.org/10.1016/j.janxdis.2022.102657

Sánchez-Polán, M., Silva-Jose, C., Franco, E., Nagpal, T. S., Gil-Ares, J., Lili, Q., Barakat, R., & Refoyo, I. (2021). Prenatal Anxiety and Exercise. Systematic Review and Meta-Analysis. *Journal of Clinical Medicine*, *10*(23), 5501. https://doi.org/10.3390/jcm10235501

Schwarze, C.E., von der Heiden, S., Wallwiener, S., & Pauen, S. (2024). The role of perinatal maternal symptoms of depression, anxiety and pregnancy-specific anxiety for infant's self-regulation: A prospective longitudinal study. *Journal of Affective Disorders, 346*, 144-153. https://doi.org/10.1016/j.jad.2023.10.035

Seng, J. S., D'Andrea, W., & Ford, J. D. (2014). Complex Mental Health Sequelae of Psychological Trauma Among Women in Prenatal Care. *Psychological Trauma: Theory, Research, Practice and Policy*, *6*(1), 41–49. https://doi.org/10.1037/a0031467

Simpson, W., Glazer, M., Michalski, N., Steiner, M., & Frey, B.N. (2014). Comparative efficacy of the Generalized Anxiety Disorder 7-Item Scale and the Edinburgh Postnatal Depression Scale as screening tools for generalized anxiety disorder in pregnancy and the

postpartum period. *Canadian Journal of Psychiatry, 59*(8), 434-440. https://doi.org/10.1177/070674371405900806

Singla, D. R., De Oliveira, C., Murphy, S. M., Patel, V., Charlebois, J., Davis, W. N., Dennis, C., Kim, J. J., Kurdyak, P., Lawson, A., Meltzer-Brody, S., Mulsant, B. H., Schoueri-Mychasiw, N., Silver, R. K., Tschritter, D., Vigod, S. N., & Byford, S. (2023). Protocol for an economic evaluation of scalable strategies to improve mental health among perinatal women: non-specialist care delivered via telemedicine vs. specialist care delivered in-person. *BMC Psychiatry*, *23*(1). https://doi.org/10.1186/s12888-023-05318-2

Skouteris, H., Wertheim, E. H., Rallis, S., Milgrom, J., & Paxton, S. J. (2009). Depression and anxiety through pregnancy and the early postpartum: an examination of prospective relationships. *Journal of Affective Disorders*, *113*(3), 303–308. https://doi.org/10.1016/j.jad.2008.06.002

Somerville, S., Dedman, K., Hagan, R., Oxnam, E., Wettinger, M., Byrne, S., Coo, S., Doherty, D., & Page, A. C. (2014). The Perinatal Anxiety Screening Scale: Development and preliminary validation. *Archives of Women's Mental Health, 17*(5), 443-454. https://doi.org/10.1007/s00737-014-0425-8

Spitzer, R.L., Kroenke, K., Williams, J.B., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: The GAD-7. *Archives of Internal Medicine, 166*(10), 1092-1097. https://doi.org/10.1001/archinte.166.10.1092

Sternheim, L. C., Fisher, M., Harrison, A., & Watling, R. (2017). Predicting intolerance of uncertainty in individuals with eating disorder symptoms. *Journal of Eating Disorders*, *5*, 26. https://doi.org/10.1186/s40337-017-0152-4

Sufredini, F., Catling, C., Zugai, J., & Chang, S. (2022). The effects of social support on depression and anxiety in the perinatal period: A mixed-methods systematic review. *Journal of Affective Disorders*, *319*, 119–141. https://doi.org/10.1016/j.jad.2022.09.005

Swanson, L. M., Pickett, S. M., Flynn, H., & Armitage, R. (2011). Relationships among depression, anxiety, and insomnia symptoms in perinatal women seeking mental health treatment. *Journal of Women's Health (2002)*, *20*(4), 553–558. https://doi.org/10.1089/jwh.2010.2371

Toscano, M., Royzer, R., Castillo, D., Li, D., & Poleshuck, E. (2021). Prevalence of depression or anxiety during antepartum hospitalization for obstetric complications: A systematic review and meta-analysis. *Obstetrics & Gynecology, 137*(5), 881-891. https://doi.org/10.1097/AOG0000000000004335

Trevillion, K., Ryan, E. G., Pickles, A., Heslin, M., Byford, S., Nath, S., Bick, D., Milgrom, J., Mycroft, R., Domoney, J., Pariante, C., Hunter, M. S., & Howard, L. M. (2020). An exploratory parallel-group randomised controlled trial of antenatal Guided Self-Help (plus usual care) versus usual care alone for pregnant women with depression: DAWN trial. *Journal of Affective Disorders*, *261*, 187–197. https://doi.org/10.1016/j.jad.2019.10.013

US Preventive Services Task Force, Curry, S. J., Krist, A. H., Owens, D. K., Barry, M. J., Caughey, A. B., Davidson, K. W., Doubeni, C. A., Epling, J. W., Jr, Grossman, D. C., Kemper, A. R., Kubik, M., Landefeld, C. S., Mangione, C. M., Silverstein, M., Simon, M. A., Tseng, C. W., & Wong, J. B. (2019). Interventions to Prevent Perinatal

Depression: US Preventive Services Task Force Recommendation Statement. *JAMA*, *321*(6), 580–587. https://doi.org/10.1001/jama.2019.0007

Vagos, P., Mateus, V., Silva, J., Araújo, V., Xavier, A., & Palmeira, L. (2023). Mother-infant bonding in the first nine months postpartum: The role of mother's attachment style and psychological flexibility. *Journal of Reproductive and Infant Psychology, 43*(2), 472-486. https://doi.org/10.1080/02646838.2023.2242379

van der Heiden, C., Muris, P., & van der Molen, H.T. (2012). Randomized controlled trial on the effectiveness of metacognitive therapy and intolerance-of-uncertainty therapy for generalized anxiety disorder. *Behaviour Research and Therapy, 50*(2), 100-109. https://doi.org/10.1016/j.brat.2011.12.005

van Heyningen, T., Honikman, S., Tomlinson, M., Field, S., & Myer, L. (2018). Comparison of mental health screening tools for detecting antenatal depression and anxiety disorders in South African women. *PLoS One, 13*(4), e0193697. https://doi.org/journal.pone.0193697

Vigod, S. N., Frey, B. N., Clark, C. T., Grigoriadis, S., Barker, L. C., Brown, H. K., Charlebois, J., Dennis, C. L., Fairbrother, N., Green, S. M., Letourneau, N. L., Oberlander, T. F., Sharma, V., Singla, D. R., Stewart, D. E., Tomasi, P., Ellington, B. D., Fleury, C., Tarasoff, L. A., Tomfohr-Madsen, L. M., … Van Lieshout, R. J. (2025). Canadian Network for Mood and Anxiety Treatments 2024 Clinical Practice Guideline for the Management of Perinatal Mood, Anxiety, and Related Disorders: Guide de pratique 2024 du Canadian Network for Mood and Anxiety Treatments pour le traitement des troubles de l'humeur, des troubles anxieux et des troubles connexes périnatals. *Canadian Journal of Psychiatry. Revue Canadienne de Psychiatrie*, 7067437241303031. Advance online publication. https://doi.org/10.1177/07067437241303031

Wake, S., Verde, A. D., Biagi, N., van Reekum, C. M., & Morriss, J. (2022). Just let me check: The role of individual differences in self-reported anxiety and obsessive-compulsive features on subjective, behavioural, and physiological indices during a checking task. *International Journal of Psychophysiology: Official Journal of the International Organization of Psychophysiology*, *179*, 43–55. https://doi.org/10.1016/j.ijpsycho.2022.06.011

Webb, R., Bond, R., Romero-Gonzalez, B., Mycroft, R., & Ayers, S. (2021). Interventions to treat fear of childbirth in pregnancy: a systematic review and meta-analysis. *Psychological Medicine*, *51*(12), 1964–1977. https://doi.org/10.1017/S0033291721002324

Weis, K.L., Walker, K.C., Chan, W., Yuan, T.T., & Lederman, R.P. (2020). Risk of preterm birth and newborn low birthweight in military women with increased pregnancy-specific anxiety. *Military Medicine, 185*(5-6), e678-e685. https://doi.org/10.1093/milmed/usz399

Wilson, E.J., Abbott, M.J., & Norton, A.R. (2023). The impact of psychological treatment on intolerance of uncertainty in generalized anxiety disorder: A systematic review and meta-analysis. *Journal of Anxiety Disorders, 97,* 102729. https://doi.org/10.1016/j/janxdis.2023.102729

Womersley, K., & Alderson, H. (2024). Perinatal mental health. *Medicine, 52*(10), 632-636. https://doi.org/10.1016/j.mpmed.2024.07.009

Yazıcı, E., Pek, T. M., Yuvacı, H. U., Köse, E., Cevrioglu, S., Yazıcı, A. B., Çilli, A. S., Erol, A., & Aydin, N. (2019). Perinatal Anxiety Screening Scale validity and reliability study in Turkish (PASS-TR validity and reliability). *Psychiatry and Clinical Psychopharmacology, 29*(4), 609-617. https://doi.org/10.1080/24750573.2018.1506247

Yelland, J., Sutherland, G., & Brown, S. J. (2010). Postpartum anxiety, depression and social health: findings from a population-based survey of Australian women. *BMC Public Health*, *10*, 771. https://doi.org/10.1186/1471-2458-10-771

Zemestani, M., Beheshti, N., Rezaei, F., van der Heiden, C., & Kendall, P. C. (2021). Cognitive behavior therapy targeting intolerance of uncertainty versus selective serotonin reuptake inhibitor for generalized anxiety disorder: A randomized clinical trial. *Behaviour Change, 38*(4), 250–262. https://doi.org/10.1017/bec.2021.16

Zimmermann, M., Julce, C., Sarkar, P., McNicholas, E., Xu, L., Carr, C., Boudreaux, E. D., Lemon, S. C., & Byatt, N. (2023). Can psychological interventions prevent or reduce risk for perinatal anxiety disorders? A systematic review and meta-analysis. *General Hospital Psychiatry*, *84*, 203–214. https://doi.org/10.1016/j.genhosppsych.2023.08.005