PROMOTING PERINATAL MENTAL HEALTH: PERSONALIZING TREATMENT DECISION MAKING STRATEGIES THROUGH DECISION-MAKING SUPPORT AND PHARMACOGENETICS

by

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Abstract

**Problem:** Depression during pregnancy affects 10-15% of women. Practice guidelines recommend that clinicians support women to make treatment decisions that are informed by the risks of both untreated depression and antidepressant use during pregnancy. However, there is minimal evidence regarding how women make these decisions or how clinicians can best support them.

**Purpose:** To advance knowledge and understanding regarding women’s decision making about perinatal depression treatment through qualitative (QUAL) and quantitative (QUANT) studies. The QUAL purpose was to develop a constructivist grounded theory, within a feminist theoretical framework, of women’s perinatal depression treatment decision making. The QUANT purpose was to test the hypothesis that women with deleterious variants in the pharmacogenes *CYP2D6* or *CYP2C19*, taking selective serotonin reuptake inhibitors (SSRIs) prenatally, would have more depression symptoms than women whose pharmacogenetic variants have been associated with normal SSRI metabolism.

**Methods (QUAL):** Semi-structured interviews were conducted with purposively-sampled, pregnant/preconception women who had experienced depression. Iterative data collection and analysis, along with theoretical sampling, in the context of reflexive journaling, peer debriefing, and expert audit, culminated in a cohesive theoretical model.

**Methods (QUANT):** Testing of *CYP2D6* and *CYP2C19* were performed as secondary analyses on two longitudinal cohorts of pregnant women taking SSRIs. The Kruskal-Wallis Test
compared mean depression scores across four predicted metabolizer groups: 1) poor, 2) intermediate, 3) extensive, and 4) ultra-rapid.

**Results (QUAL):** Participants’ \((N=31)\) decision-making processes were complex and dynamic, and highly influenced by contextual factors - particularly stigma, patriarchy, privilege, and their emotional/cognitive environments. Participants navigated towards a decision, in a non-linear manner, between three clusters of decision-making activities: 1) seeking information, 2) making sense of information, and 3) self-soothing.

**Results (QUANT):** There were no significant differences between mean depression scores across the four metabolizer groups \((N=83; \text{H}(3)=.73, p=.87)\).

**Conclusions:** The grounded theory provides insight into how women have made this decision, which can be useful both practically and emotionally. Evidence from the pharmacogenetic study clarifies the limitations of this field, which is especially vital in this era of direct-to-consumer genetic testing. Together, they can support patient-oriented decision making regarding perinatal maternal mental health.
Lay Summary

Women deciding about whether to take antidepressants during pregnancy find the process to be difficult. They try to reach a decision through a process that moves back and forth between information seeking, making sense of information, and working to ease the burden of anxiety, guilt, and fear that the decision triggers. An important part of the decision is what antidepressant to take, and at what dose. Genetic tests might help guide this decision, but this study found that there isn’t enough evidence for genetic tests to be helpful in making this decision, at the moment. In this dissertation, 31 women shared their stories of making this decision, and genetic testing was done for 83 other women who were taking antidepressants during pregnancy. From women’s stories, we developed a model of decision making. This model can be used by women and their care providers to help when making this decision.
Preface

All work presented in this original, intellectual contribution by C. Hippman was conducted with the support of the Translational Psychiatric Genetics Group (TPGG), led by Dr. Jehannine Austin, based at the British Columbia (BC) Mental Health and Substance Use Services Research Institute (BC Children’s and Women’s Hospital campus).

Chapter 1. Versions of sections in the Literature Review have been published:


For the first two manuscripts, I drafted the works and my co-authors revised them critically for important intellectual content. They both arose from independent study courses completed as part of my PhD. For the Hippman and Davis (2016) manuscript, we contributed equally to the qualitative analysis [which is not part of this dissertation], and the writing of the manuscript.

Chapter 2. Preliminary results from this project were presented as abstracts at the 2018 Society for Medical Decision Making conference [Hippman, C., Ryan, D., Balneaves, L.G., Austin, J. Deciding whether to take antidepressants during pregnancy: A grounded theory. *Medical
Decision Making. 2019. 39(1). e98.], at the 2019 Qualitative Health Research conference [Hippman, C., Ryan, D., Balneaves, L.G., Austin, J. “The biggest decision I’ve ever made”: A grounded theory of decision making regarding antidepressant use in pregnancy. International Journal of Qualitative Methods. 2020. 19. e30.], and at the 2019 National Society of Genetic Counselors conference [Hippman, C., Ryan, D., Balneaves, L.G., Austin, J. Deciding whether to take antidepressants during pregnancy: A grounded theory. Presented as an oral presentation at the National Society of Genetic Counselors 38th Annual Education Conference, November 5-8, 2019. Published on the NSGC website.]. I was the lead investigator for this project, responsible for all major decisions in conception, design, data collection, data analysis, and presentation of results. Balneaves was the lead supervisor on this project and was involved throughout, including acting as expert auditor for the coding framework development and overall data analysis. Ryan supported recruitment efforts for the study, provided clinical review of the data analysis, and revised the abstracts critically for important intellectual content. Austin made important intellectual contributions to study design, data analysis, and presentation of results. Interview transcription was performed by Transcript Heroes or volunteers of TPGG. The study was approved by the UBC/Children’s and Women’s Hospital ethics board (H15-01687).

Chapter 3. None of this work has been published, to date. I was the lead investigator for this project, responsible for all major decisions in conception, design, data analysis, and presentation of results. I contributed significantly to data collection for cohort A [Austin lab], in collaboration with past and present members of TPGG. Study protocol for cohort A was approved by the UBC/Children’s and Women’s Hospital ethics boards (H06–70145). Data for cohort O were provided by Dr. Tim Oberlander and Ursula Brain. Study protocols for cohort O were approved
by the UBC/Children’s and Women’s Hospital ethics boards (cohort O1: H00-70500; cohort O2: H05-70629). Genotyping of DNA samples was provided by Dr. Andrea Gaedigk’s lab for cohort O, and by Dr. Colin Ross’ lab for cohort A. I performed variant interpretation of the genotyping results, with support from Dr. Andrea Gaedigk and Dr. Galen Wright. I conducted all statistical analyses.
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List of Abbreviations

ANCOVA = Analysis of Covariance
ASD = Autism Spectrum Disorder
CBT = cognitive behavioural therapy
CI = confidence interval
CNV = copy number variation
CPIC = Clinical Pharmacogenetics Implementation Consortium
CYP450 = cytochrome P450
DBT = dialectical behaviour therapy
DDD = defined daily dose
DM = decision making or decision-making
DPWG = Dutch Pharmacogenetics Working Group
EM = Extensive metabolizer
EPDS = Edinburgh Postnatal Depression Scale
IM = Intermediate metabolizer
IUGR = Intrauterine growth restriction
kg = kilogram
M = mean
mg = milligram
PCR = polymerase chain reaction
PDD = prescribed daily dose
PM = Poor metabolizer
PNAS = Poor neonatal adaptation syndrome

PPH = Persistent pulmonary hypertension

RFLP = restriction fragment length polymorphism

RMH = Reproductive Mental Health

rs = reference SNP [cluster ID number]

SD = standard deviation

SNP = single nucleotide polymorphism

SSRI = selective serotonin reuptake inhibitor


UM = Ultra-rapid metabolizer

XL-PCR = long-range PCR
Glossary

**Analysis of Covariance (ANCOVA):** Method to test whether the means of a dependent variable (in this case – depression scores) are statistically different across a group variable (in this case – predicted metabolizer group), while controlling for the impact of potential confounder variables (in this case – SSRI dose, weight, and gestational age).

**Disconfirmatory evidence:** Evidence that is inconsistent with a given hypothesis or conjecture.

**Ulysses agreement:** A mechanism by which an individual with a history of mental illness outlines actions to be taken, or not taken, in response to articulated observable behaviours, or resulting events, by a given individual in the interests of partnering to protect their mental health (https://www.bcss.org/family-advocacy/ulysses-agreement/).
Acknowledgements

During my PhD, I received salary support from a Frederick Banting and Charles Best Canada Graduate Scholarship (CGS-D), a UBC Killam Doctoral Scholarship, a UBC Four Year Fellowship Award, and Dr. Jehannine Austin. I received operational funding through a competitive application process in support of my PhD qualitative study from the UBC School of Nursing’s Sheena Davidson Nursing Research Fund.

I sincerely thank everyone who helped me with recruitment for the qualitative study- the staff of the Reproductive Mental Health program, Angela Inglis and Emily Morris in the Adapt clinic, Caitlin Slomp with TPGG, and volunteers of TPGG who put up posters around the community. I extend deep gratitude to all the TPGG volunteers and the volunteer chief, Rolan Batallones, for assistance with interview transcription and saving me from starting from scratch with a new reference manager system when my laptop died in late 2018.

My quantitative study embodies the spirit of “it takes a village”, and it wouldn’t have been possible without support from countless individuals. I regret not being able to name them all, but I don’t even know all the names of everyone who has contributed to these longitudinal cohorts over the years. Cohort A was a TPGG team effort (acknowledged below). For cohort O, I offer my earnest thanks to Dr. Tim Oberlander and Ursula Brain. I am delighted to have had the chance to collaborate with you again, and look forward to continuing to partner in our efforts to improve outcomes for moms and babies affected by depression. I consider myself very fortunate to have met Dr. Andrea Gaedigk through this research and hope to meet in person some day! Dr.
Gaedigk’s meticulous work and reliably rapid communication, in combination with her warm and supportive demeanor, made the distance between Vancouver and Kansas City feel negligible. I am very grateful to Dr. Colin Ross, Michelle Higginson, Fudan Miao, and Dr. Galen Wright for their extremely timely and careful work genotyping cohort A; it was a pleasure to work with you.

I thank Dr. Deborah Money, Dr. Lori Brotto, and the Women’s Health Research Institute, for their encouragement and support of my research career, and for fostering a community of researchers passionate about women’s health.

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I entered my PhD excited to expand my knowledge of research methodologies and challenge myself to move outside my comfort zone. The UBC Interdisciplinary Studies Graduate Program was the perfect place for me to achieve these goals and I thank everyone who has dedicated themselves to the creation and protection of this learning space. I thank Susan Dahinten for helping me to advance my statistics skills in a nurturing environment. I thank Susan Cox for the chance to expose my assumptions and grapple with difficult questions regarding knowledge creation, while at the same time connecting me to a community of like-minded individuals and showcasing ways in which my love of art and beauty can harmonize with my love of research.
I thank my PhD committee members for being my cheerleaders on my path towards saying “no” and channeling my energy strategically, rather than haphazardly. Thank you to Dr. Corey Nislow for keeping me in touch with the big picture and encouraging me to share rough drafts and overcome my perfectionist instincts. Thank you to Dr. Deirdre Ryan for your clinical wisdom, prioritizing our work together, and warm reminders to care for myself. Thank you to Dr. Lynda Balneaves for teaching me to have conviction in my judgment and decisions as a researcher, the creativity you bring to qualitative analysis, and your wholehearted support of my feminist approach.

I would like to acknowledge the Translational Psychiatric Genetics Group for their manifold support, insight, guidance, and commitment. It has been a privilege to complete my PhD in a culture that is nurturing, inspiring, and which emphasizes helping each other to take advantage of growth opportunities.

I thank all of my friends and family for their support over the years of my PhD. Pop culture suggests that asking a PhD student about their progress should be avoided under all circumstances, but it meant a lot to me that you tried to grasp what I was going through and asked for updates.

The power differentials embedded within the PhD process mean that a supervisor has the power to make or break the experience. Jehannine – you made mine a festival of feminism. It’s strange to think back to a conversation that we had near the beginning of my PhD, when I was puzzling over what theoretical framework I wanted to use for my research. After listening to my stream of
consciousness, you said: “it sounds like feminist theory to me”. YES! This is just a small example of one of your super powers – listening, seeing what someone needs, and helping them to see it too. When I asked in my UBC genetic counselling program interview in 2005 if the program had someone in the area of psychiatric genetic counselling, and they said there was you, I hoped we could work together. You’ve exceeded my wildest expectations, and I look forward to continuing to support each other through many future growth opportunities. You challenge; you inspire; you nurture. Thank you.

Finally – to Nick – you’ve supported me in three births since 2016, and I can’t imagine a better partner for my life’s work. Whenever I’ve talked to people about my PhD, I’ve shared my gratitude that I’ve been supported by you to focus on my research full-time (well, as full-time as possible in the context of birthing and raising two children). Often in these conversations, I have focused on the financial support you’ve given, but it’s really the emotional and practical support that made the biggest difference. In my wedding vows, I promised to “make time for us - which will mean saying no to some of the millions of things I want to do”. Developing strategies for screening requests and practicing saying “no” has been a vital part of my PhD experience. It has become easier as our lives continue to become richer and fuller. As I said when we married: you are the love of my life, my best friend, and I thank you for all that you give me.
Dedication

I dedicate this dissertation to all women and genderqueer individuals who have faced, are facing, or will face, the decision regarding how to care for their mental health, including whether to take antidepressants, during pregnancy.

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Chapter 1: Introduction
Research purpose & questions

Purpose: To generate data to support women making decisions about antidepressant use during pregnancy.

Background: Depression affects 10-15% of pregnant women; untreated it impacts a woman’s quality of life and puts her at risk of loss of life through suicide. In pregnancy, these risks are compounded by potential risks to fetal development and infant outcomes (e.g., preterm birth). Selective serotonin reuptake inhibitors (SSRIs) can successfully treat depression. The conundrum is that using SSRIs prenatally also carries risks for both mother (e.g., postpartum hemorrhage) and baby (e.g., poor neonatal adaptation syndrome). At the population level, the risks of untreated depression and SSRI use during pregnancy appear to be comparable, such that clinical guidelines recommend supporting women to make an informed decision regarding treatment for depression during pregnancy. However, there is a paucity of published data regarding how women make these decisions or how best to support them. Further, women are often making these decisions without any data on the likelihood that a given antidepressant, at a given dose, will alleviate their depression symptoms in the context of pregnancy. Genetic differences in CYP2D6 and CYP2C19 impact SSRI response, for example, but current guidelines for pharmacogenetically-guided SSRI treatment may need to be adapted for pregnant women given physiological changes of pregnancy.

Questions: In service of the research purpose, I conducted two studies addressing the following research questions:

1) How do women decide whether or not to take antidepressants during pregnancy?
2) For women taking SSRIs during pregnancy, do scores measuring depression symptoms differ significantly depending on which variations they have in the genes \textit{CYP2D6} and/or \textit{CYP2C19}?

**Research objectives and aims**

**Objective 1:** To understand the process of decision making (DM) for women considering prenatal antidepressant use.

**Aims:**

1) Conduct qualitative interviews with pregnant women with a history of depression: those using SSRIs (n=15) and not using SSRIs (n=15).

2) Use constructivist grounded theory methods to develop a DM theoretical model.

**Objective 2:** To test whether depression symptoms during pregnancy, amongst women taking SSRIs, differed depending on which variants women had in the \textit{CYP2D6} and \textit{CYP2C19} genes.

**Aims:**

1) Perform variant interpretation analyses to predict phenotype (poor metabolizer (PM); intermediate metabolizer (IM); extensive metabolizer (EM); or ultra-rapid metabolizer (UM)) for \textit{CYP2D6} and \textit{CYP2C19} pharmacogenetic results for two cohorts of women taking SSRIs during pregnancy.

2) Compare mean depression scores across the four predicted phenotype groups using ANCOVA, with SSRI dose, weight, and gestational age as covariates ($\alpha=0.05$).
Paradigmatic orientation

Paradigmatic orientation describes assumptions underlying a researcher’s approach; namely assumptions of: ontology, epistemology, methodology, and axiology. Ontology describes a researcher’s perspective on the nature of reality – whether there exists one reality or ‘truth’. Epistemology describes the researcher’s view of knowledge – whether it is possible to know ‘reality’ or ‘truth’. Methodology describes the processes a researcher uses to gain knowledge – that is, the processes a researcher believes will allow them to gain knowledge. Axiology describes a researcher’s values, and how these values influence their ways of knowing/interacting with knowledge.

I don’t have just one paradigmatic orientation through which I relate to research. While I would say that my values/axiology are consistent, my beliefs about ontology and epistemology vary depending on type of phenomenon, and my views on methodology vary to align with my beliefs about ontology and epistemology, given the phenomenon of interest. For example, in this dissertation research, I would characterize one phenomenon of interest as human experience – particularly, of DM regarding antidepressant use in pregnancy. In this case, I don’t believe there is one ‘reality’ or ‘truth’, and I believe that it is only possible, for the myriad realities in existence, to gain knowledge/understanding that is limited, partial, and tentative. Hence, the philosophical theory of constructivism aligns well with my ontological and epistemological perspective. In constructivist theory, realities are multiple, specific, local, co-constructed, and knowledge of them is co-created by researcher and participant. The methodology of constructivist grounded theory focuses on meaning-making and honours the diverse experiences of participants. It also emphasizes creativity in the development of the theory and in its
presentation. In contrast, “objectivist grounded theory accepts the positivistic assumption of an external world that can be described, analyzed, explained, and predicted” (p. 274). Researchers implementing objectivist grounded theory often follow a set of prescriptive ‘rules’ with the goal of uncovering one ‘true’ core category that exists in the data, and developing a theory that can explain and predict experience for at least a subset of the populace. Constructivist grounded theory is not only a better fit with my ontological and epistemological perspective on human experience, but also my axiology. As a researcher, I value making connections, respecting individuals’ uniqueness, sharing knowledge for the good of many, and creating things of beauty. For me, a successful grounded theory is one which has a rich enough ground that it can offer a window into diverse experiences, and a theory, brought into relief against the ground, that supports people to connect with common aspects of the phenomenon, and perhaps shift their perspective – in short, I aspire to provide inspiration and comfort through the connections that I make: 1) with women, and 2) between their stories.

Another phenomenon of interest in this dissertation research lies at the intersection of the human experience of mental illness and its relationship to the physical nature of women’s genetic composition. I believe in the singular reality of each individual’s genetic structure that I believe can be described, although it is complex and only partially understood at this time. I also believe that mental illnesses, such as depression, are caused by a combination of genetic and environmental factors. Thus, I believe not only that there are genetic differences that can be identified, but also that these differences will have biological consequences that are predictable (theoretically, if not in practice yet), and that these factors will contribute to women’s experience of depression. Furthermore, I believe that medication can act on these biological factors and have an impact on women’s experience of depression, and that there are also identifiable genetic
variations that can influence the action of the medication. While I believe that every woman’s experience of depression is unique and only partially know-able, I believe that the strategies that the field of psychiatry has established to access experiences of depression, and areas of commonality in those experiences, are sufficient to allow an understanding that approximates ‘reality’. For this phenomenon, then, I would say that my ontological and epistemological viewpoint aligns with the philosophical theory of postpositivism – that there is a reality, although it is imperfectly apprehensible. Hypothesis testing, then, is an appropriate methodology for this phenomenon.

Altogether, my approach aligns with “methodological pluralism”, which embraces diversity in methodological approaches, and “is usually based on an explicitly assumed epistemological pluralism (i.e., there are many legitimate types and sources of knowledge).”3(p. 20). Further, methodological pluralism is often employed in the context of a consciously articulated, coherent set of values. I see a researcher’s values as playing a foundational role in the choice of research questions pursued, and then the construction of the design of the research program. I believe that assuming epistemological pluralism, and combining constructivism and postpositivism specifically, recognizes the complexity of the human condition and enables a deeper, richer understanding of phenomena (in this case, decision making).

**My position as an insider**

Reflexivity describes researchers’ awareness of their own impact on, and relationship to, the research.4,5. There is general consensus in the qualitative research literature that engaging in reflexivity is a defining characteristic of rigorous research practice6–11, and a view that is gaining strength is that reflexivity is also a mechanism for promoting ethical research practice4,12–14. The personal positioning of the researcher, in terms of their background and relationship to the topic,
is particularly important in constructivist qualitative research, and also in feminist research. Constructivist analyses prioritize making meaning in the interpretation of narratives while remaining conscious of one’s own biases and perspectives. Thus, it is not necessary to avoid bias; indeed, this is impossible given the personal nature of the data and analytic process. Rather, it is imperative to be aware of bias and transparent with readers such that they may make their own interpretations.\textsuperscript{15,16}

I approached my dissertation conscious of many aspects of my identity – my position as a white, cis-gender, heterosexual women with a great deal of privilege, including racial, educational, class, economic, and geographic. Perhaps the aspect of my identity of which I was most conscious, however, was my position as an insider relative to this specific research area. I have lived experience of making the decision of whether to take antidepressants during pregnancy. In fact, I made this decision multiple times during my PhD, while trying to conceive in 2015/2016, during my pregnancy in 2016, and then while trying to conceive in 2018/2019, and during my pregnancy in 2019. These time periods overlapped with the times during which I was recruiting and conducting the qualitative interviews, and concurrently engaging in the grounded theory analysis for my dissertation.

An autobiographical interlude

During my first year of the PhD program, I was beginning to grapple with the decision about taking antidepressants during pregnancy as I contemplated trying to conceive. I had been taking antidepressants for approximately five years at that point to help manage my symptoms of depression and anxiety, and found them incredibly helpful.
Reflexive journal excerpt – March 2015, remembering how I felt shortly after I started taking antidepressants:

_It has felt miraculous to me – after years of avoiding medication, feeling like I should be able to manage without – I feel some relief from the tension and haven’t had a panic attack in months. I want to tell everyone that you don’t have to struggle on your own – there is medication that can WORK! But then I don’t, because people might judge me._

Reflexive journal excerpt – April 2015, trying to decide about taking antidepressants during pregnancy:

_I want a baby. I mean I’m somewhat terrified of becoming a parent, but I’m also really excited about that possibility (sigh). I spend so much time thinking about, and talking about, mental illness and antidepressant medication and pregnancy, but in general, more abstract terms. Whenever I try to turn my thoughts to how that knowledge might apply to me, it’s like I’m in the dark, trying to grasp something very slippery that I can’t see. Even when I get close, it slithers away. Then I tell myself that it’s ok – I can try again another time, and as soon as I give myself permission, myriad thoughts crowd around, demanding my attention._

_Ok. Let’s try thinking this through more gently – not trying so hard. Breathe in. Breathe out. Relax and let your body feel heavy, tension draining away. Create an openness in your mind. You know that taking medication during pregnancy has some risks. You know that experiencing panic attacks during pregnancy has some risks. I could feel guilty either way. I probably will._
I’m very good at it (rueful smile). This is the point where I usually stop because I feel like the risks of both are about equal, and so I feel paralyzed. Like seeing the spinning ball of death on my Mac laptop when a program crashes. Relax. Breathe. Try a new question: Am I more worried about one of those possibilities? I may be marginally more worried about experiencing panic attacks during pregnancy and how that might impact me and the baby. There is a third possibility that tentatively raises its hand – that I stop taking medication and manage my anxiety so that I don’t have panic attacks during pregnancy. Could I do that? I feel like I’ve been doing a lot better, and I have lots more insight and strategies for reducing my anxiety. Oh (surprised)! I am scared to stop taking antidepressants. I’m imagining taking away the antidepressants, which have given me relief and comfort. I sit with the fear. My stomach is clenched in cold knots. What if the panic attacks come back? Breathe. Relax. I focus on my breath entering my nose and travelling down my throat into my lungs. My lungs expand and my shoulders release. The knots loosen slightly. I remember my meditation practice. I am centered and grounded. I tell my body that everything is ok. I believe I am in control. I want to try managing my anxiety without medication. Running helps. Meditation helps. I have great relationships. My support people know the red flags to look out for so that they can bring more help.

Medication was like a miracle.
Between this rock and hard place.
I’ve been there! But can I be trusted?
On the edge. Can I take the leap?
I feel safe.
And I let go.

Reflexive journal excerpt – May 2015, stopped taking antidepressant because I thought I might be pregnant, re-thinking that decision:
It’s been two days since I’ve believed that I am pregnant. Call with Jehannine – stopped taking antidepressant. Nick [my husband] questions – is that the best idea? Suggests talking to JA. Call - highly unlikely that I am actually pregnant and even if I was, would taking antidepressant be the worst thing? In scenario that I am not pregnant (which is most likely), would I stop taking antidepressant? Particularly immediately before travelling to Brazil by myself to talk at a conference. No. Re-started antidepressant (only missed one day).

Reflexive journal excerpt – November 2015, reflecting on the interaction I had with my family doctor regarding DM about antidepressants in pregnancy:

I stopped taking birth control in August and have since had my period three times, each time a disappointment. I went to see my family doctor to get a prescription refill and to ask for a referral to the Reproductive Mental Health (RMH) program at the same time. After talking to the resident, my family doctor came in and asked me if I was currently seeing a counselor. I am not, and she asked if I might be interested in it. I said that I am not opposed to it, but that I felt that my previous counselor and I had accomplished all that we could together and so that I wouldn’t particularly like to go back to her (I know what she’ll say – I need to make more time for myself, prioritize myself, not over-schedule myself). My family doctor offered me recommendations of counsellors that other patients have found helpful (one of whom happens to be a woman who was in my tap class last year. As a side note, I feel a bit weird about going for counselling with people in the tap community. The counsellor available to students on the Oak Street campus is also a tapper at the Rhythm Room- unless that’s changed – and I don’t feel 100% comfortable
with that). Then my family doctor was saying how “if you start trying to get pregnant, then you might want to re-start counselling to have as many supports in place as possible”, which I know is what the guidelines recommend, but it frustrated me that she didn’t seem to understand that I had already discussed with her that I have been actively trying to conceive – this is not a hypothetical plan. I reinforced the fact that we are actively trying and she finally seemed to understand the urgency and started reviewing my medication dose (lowest possible) and said how I could maybe try coming off it – starting by taking it every other day maybe and seeing how I feel, “because if you don’t need to be on medication, it’s better not to be”. I know, again, that this is what the guidelines say, but she didn’t ask me anything about my life circumstances or engage in a conversation about whether it would be a wise time to stop taking medication for me.

If she’d asked, I would have told her that I have my comprehensive exams and oral dissertation proposal defense scheduled for early next year, about which I am quite anxious (and anticipate rising levels of anxiety). As it was, I entered that state that happens when I’m on my own at a doctor’s appt and the doctor is saying something that I don’t fully agree with, where I become kind of stunned and incapable of advocating for myself. So I found myself agreeing to try stopping the medication and to call her in a couple of weeks to tell her how it’s been going. I was a bit shaken up, and as I left, I was questioning whether I should stop taking the medication. It took me several hours to calm down and think it through and then re-affirm my decision to keep taking the medication. Before I left the appointment, I had asked again about a referral to RMH, and she had said that she didn’t think they accepted referrals for people who weren’t pregnant, but that she would look into it. The next day, I double checked the RMH website and confirmed that they do medication consults pre-conception, so I called back my family doctor’s office and asked them to make the referral and mark it ‘urgent’. I have since left a voicemail at RMH and
asked them to add me to a cancellation list and to let me know if they don’t receive a referral.

Sadly, a take away message when I left my family doctor’s office was that I don’t have a health care provider that will have my back – she is just following the guidelines like a bit of a robot. I want an HCP who is caring for ME, not patient number 9 that day. I also want to talk to someone who knows MORE than I do about antidepressant use and mental health in pregnancy, not LESS (which was the case here).

When I got home, I talked to Nick about it, and he validated my frustrations with our family doctor. I said that I wanted someone to tell me what I already know and what I can tell myself – to validate my choice to take the medication. I told him what I know the literature says and what the limits are – what is not known. I also said how I know I could call the Motherisk program in Toronto but that I know from reading their publications and listening to their representatives present, that they are biased TOWARDS medication (e.g., when they published about counselling women that Paxil does not increase risk for birth defects at the same time as the evidence was emerging about increased risk for heart defects) and that I know they would tell me what I want to hear, but that I wouldn’t find that satisfying because I don’t trust them. I need to hear from someone that I consider an expert, with whom I have a trusting relationship, that taking Pristiq during pregnancy is ok for me.

This is echoed in the literature – the publication by Nygaard talked about women’s need for validation of their decision, particularly when their decision is to take the medication.
I talked to Jehannine about how ironic it is that I am a “non-compliant” patient – adamantly continuing to take my antidepressant against medical advice. We wondered how many people do this – it’s probably quite rare.

Makes me think about shared DM and how providers might think they have patients agreeing to a mutual decision, when actually the patient has felt disempowered by the interaction.

I passed my comprehensive exam on January 28, 2016. I had my appointment at RMH on February 17, 2016, at which my psychiatrist validated my decision to continue antidepressants during pregnancy and, in fact, suggested increasing the dose (which I agreed was a good idea, and did in follow up). We submitted our CIHR project grant before the March 1, 2016 deadline. I found out that I was pregnant on March 12, 2016. I have continued to take my antidepressant at the higher dose since then.

Advantages and disadvantages of insider status

It has been argued that researchers will always be both insiders and outsiders in their research context, because humans are multi-faceted, and researchers will share some characteristics with their participants and not others. Some authors suggest that by virtue of engaging in the research, researchers cultivate a hybrid position in which they are neither fully an insider nor fully an outsider.

As discussed by Merton (1972), insider status can be both advantageous and disadvantageous to a researcher: advantageous in being able to create a credible account that resonates with participants and having insight into questions that prove fruitful; disadvantageous in having an extra challenge to separate the researcher’s own biases in interpretations and having
to avoid the scenario of the researcher’s preconceptions masquerading as research findings. Arguably, this disadvantage is more detrimental to research conducted within a positivist or postpositivist paradigm. As mentioned, constructivism does not require separation of researcher biases in the analysis. The advantage of greater insight into the research area can also be conceptualized as enhancing a researcher’s theoretical sensitivity in the case of grounded theory methodology, as alluded to by Plummer and Young (2010)\textsuperscript{22}.

Other advantages of conducting research as an insider that have been articulated include: minimization of the power differential between researcher and participant, greater rapport, and increased depth of participant disclosure, all of which create data that are more rich and textured\textsuperscript{20,23}. On the other hand, additional disadvantages that have been argued include: participant discomfort with disclosing to an insider (preferring the anonymity of an outsider); failure to challenge participants and themselves to dig deeper into the data, rather than relying on implicit and assumed knowledge; and an added layer of researcher vulnerability.

In terms of participant discomfort with disclosing to an insider, it is important to note that I had control over the choice to reveal my position as an insider with respect to my experience of depression and deciding to take antidepressants during pregnancy. I only chose to disclose these aspects of my life if I felt that the disclosure would support participants to engage openly in the interview, and that my own motivation for sharing was in the interests of the participant, rather than my own interests. I had less control over disclosing the layer of my insider status with respect to my experience of pregnancy when I was conducting interviews while pregnant. I still had a choice over disclosure for interviews conducted by phone, but my pregnancy was evident to those that were in person during my second and third trimesters.
In order to address the risk of reliance on shared or assumed knowledge, particularly with respect to pregnancy when I did not have a choice regarding self-disclosure, I maintained a heightened awareness of my beliefs and values – central to constructivism and feminism – that women’s experiences are varied and it is important to remain open and curious to hear women’s unique stories. I believed it was an honour and privilege when women offered me insight into their worlds, and that I would be doing them a disservice if I did not do my utmost to create space for them to share their stories.

With respect to the risk of increased researcher vulnerability, and potential harms to my own health\textsuperscript{24,25}, these were discussed candidly at the outset of the research with my PhD committee. In addition to keeping a reflexive journal and peer debriefing, I put the following measures in place to support my mental health: I started working with a therapist who is completely external to UBC/RMH/the tap community (with whom I continue to work), I worked with psychiatrists at RMH during and after both pregnancies, and I created a Ulysses agreement with Dr. Austin outlining signs that she can identify and ways in which to respond to help me in managing my mental health.
Literature review

Depression

Mental illness costs Canada at least $50 billion annually\textsuperscript{26–28}. Depression is the leading cause of disability worldwide\textsuperscript{29}, and in a given year, \textasciitilde5\% of Canadians experience depression\textsuperscript{30}. It is characterized by persistent feelings of sadness and/or loss of interest in things that were formerly pleasurable, in addition to somatic symptoms (e.g., changes to appetite or sleep) and cognitive symptoms (e.g., difficulty concentrating)\textsuperscript{31}. Untreated depression has dramatic, negative impacts on both an individual level in terms of quality of life, and sometimes loss of life through suicide, as well as on a population level, in terms of lost work productivity and health service costs\textsuperscript{32}. Fortunately, many treatment options for depression have demonstrated efficacy, including medications\textsuperscript{33}, psychotherapy\textsuperscript{34}, electroconvulsive therapy\textsuperscript{35}, deep brain stimulation\textsuperscript{36}, and complementary and alternative medicine options\textsuperscript{37,38}. Antidepressants can effectively treat depression\textsuperscript{39}, and prescriptions for them have increased dramatically since the approval of SSRIs, including amongst women of childbearing age\textsuperscript{40,41}.

Depression during pregnancy

Depression disproportionately affects women (who are 1.5-2 times more likely to experience depression than men\textsuperscript{26,42}), and affects 10–15\% of pregnant women\textsuperscript{43–45}. Suicide is a leading cause of death during pregnancy and in the first year postpartum\textsuperscript{46–48}. Less extreme, but nonetheless important, negative consequences of untreated depression during pregnancy exist not only for the mother (impacting quality of life, for example), but also for the baby (e.g., increasing risk for preterm birth)\textsuperscript{49}. Taking SSRIs mitigates these risks by lowering the chance
for depression relapse\textsuperscript{50}, and so they are commonly prescribed; in 2006, SSRI prescriptions were filled for 4.5\% of pregnant women in British Columbia\textsuperscript{51}. Similar rates of SSRI use during pregnancy have been reported more recently; between 2002 – 2011, SSRI prescriptions were filled for 2.5-5\% of pregnant women (depending on pregnancy trimester) in British Columbia\textsuperscript{52}, and between 2006 – 2011, SSRI prescriptions were filled for 5.1\% of pregnant women with private insurance in the US\textsuperscript{53}. However, antidepressant use may have risks for both mother (e.g., postpartum hemorrhage\textsuperscript{54,55}), and baby (e.g., poor neonatal adaptation syndrome\textsuperscript{56}).

Tables 1.1 and 1.2 summarize results from meta-analyses that have evaluated the impact of exposures during pregnancy (to depression or medications for depression) on the fetus/child. It is important to note that, though statistically significant differences between groups have been identified, the magnitude of these differences is generally considered to be small and of questionable clinical significance\textsuperscript{57–61}, and/or potentially confounded by indication\textsuperscript{60,62–65}. Because the risks of prenatal depression and prenatal antidepressant use are comparable on a population level, clinical guidelines recommend supporting women to make informed prenatal depression treatment decisions\textsuperscript{66–70}. 
Table 1.1. Summary of meta-analyses evaluating impact of depression- and treatment-related exposures during pregnancy on the fetus/child

<table>
<thead>
<tr>
<th>Meta-analysis</th>
<th>Exposure¹</th>
<th>Impact on fetus/child</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grote et al., 2010³¹</td>
<td>Untreated depression</td>
<td><strong>No statistical association with:</strong></td>
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<td></td>
<td></td>
<td>1) Intrauterine growth restriction (IUGR)</td>
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<td></td>
<td></td>
<td><strong>Statistically significant association with:</strong></td>
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<tr>
<td></td>
<td></td>
<td>1) Low birth weight</td>
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<td></td>
<td></td>
<td>2) Preterm birth</td>
</tr>
<tr>
<td>Ross et al., 2013⁵⁷</td>
<td>Antidepressants</td>
<td><strong>No statistical association with:</strong></td>
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<tr>
<td></td>
<td></td>
<td>Miscarriage</td>
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<td></td>
<td></td>
<td><strong>Statistically significant association with:</strong></td>
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<tr>
<td></td>
<td></td>
<td>1) Lower gestational age at delivery</td>
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<tr>
<td></td>
<td></td>
<td>2) Lower birth weight</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3) Lower APGAR scores</td>
</tr>
<tr>
<td>Grigoriadis et al., 2013⁵⁸</td>
<td>SSRIs</td>
<td><strong>No statistical association with:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Persistent pulmonary hypertension (PPH) when SSRIs taken in ‘early pregnancy’ (~ &lt; 20 weeks)</td>
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<td></td>
<td></td>
<td><strong>Statistically significant association with:</strong></td>
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<td></td>
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<td>PPH more frequent when SSRIs taken in ‘late pregnancy’ (~ &gt; 20 weeks)</td>
</tr>
<tr>
<td>Grigoriadis et al., 2013⁵⁶</td>
<td>Antidepressants</td>
<td><strong>Statistically significant association with:</strong></td>
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<tr>
<td></td>
<td></td>
<td>Poor neonatal adaptation syndrome (PNAS)</td>
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<tr>
<td></td>
<td></td>
<td>a. Respiratory distress</td>
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<td></td>
<td></td>
<td>b. Tremors</td>
</tr>
<tr>
<td>Grigoriadis et al., 2013⁵⁹</td>
<td>Untreated depression</td>
<td><strong>No statistical association with:</strong></td>
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<tr>
<td></td>
<td></td>
<td>1) Birth weight</td>
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<tr>
<td></td>
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<td>2) Neonatal intensive care unit admissions</td>
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<td></td>
<td></td>
<td>3) Preeclampsia</td>
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<td></td>
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<td>4) APGAR scores</td>
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<td></td>
<td></td>
<td>5) Gestational age at delivery (mean difference)</td>
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<td></td>
<td></td>
<td><strong>Statistically significant association with:</strong></td>
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<tr>
<td></td>
<td></td>
<td>1) Less frequent breastfeeding initiation</td>
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<td></td>
<td></td>
<td>2) Preterm delivery</td>
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</tbody>
</table>

Notes. ¹Due to limitations in the literature, ‘untreated depression’ refers to depression that is not being treated with medication
<table>
<thead>
<tr>
<th>Meta-analysis</th>
<th>Exposure(^1)</th>
<th>Impact on fetus/child</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grigoriadis et al., 2013(^{59})</td>
<td>Antidepressants (specifically including sub-analyses for fluoxetine and paroxetine when possible)</td>
<td><strong>No statistical association with:</strong></td>
</tr>
<tr>
<td>((N=3,181,046; 27<del>studies</del> included))</td>
<td></td>
<td>1) Congenital malformations - general</td>
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<td></td>
<td></td>
<td>2) Major congenital malformations</td>
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<td></td>
<td></td>
<td><strong>Statistically significant association with:</strong></td>
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<td></td>
<td></td>
<td>Cardiac malformations</td>
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<tr>
<td></td>
<td></td>
<td>a. Septal heart defects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b. Paroxetine</td>
</tr>
<tr>
<td>Myles et al., 2013(^{72})</td>
<td>SSRIs</td>
<td><strong>No statistical association with:</strong></td>
</tr>
<tr>
<td>((N=2,638,602; 29<del>studies</del> included))</td>
<td></td>
<td>Congenital malformations – Citalopram &amp; Sertraline</td>
</tr>
<tr>
<td>McDonagh et al., 2014(^{73})</td>
<td>Antidepressants</td>
<td><strong>Statistically significant association with:</strong></td>
</tr>
<tr>
<td>((N=5,649,915; 57<del>studies</del> included))</td>
<td></td>
<td>1) Major congenital malformations – Fluoxetine &amp; Paroxetine</td>
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<tr>
<td></td>
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<td>2) Cardiac malformations - Paroxetine</td>
</tr>
<tr>
<td>Huang et al., 2014(^{74})</td>
<td>Antidepressants</td>
<td><strong>Statistically significant association with:</strong></td>
</tr>
<tr>
<td>((N=3,063,499; 28<del>studies</del> included))</td>
<td></td>
<td>1) Neonatal convulsions</td>
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<td>2) Preterm birth</td>
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<td>3) Breastfeeding outcomes</td>
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<td>4) Fetal growth</td>
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<td>5) Major congenital malformations (SSRIs as a group)</td>
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<td>6) Cardiac malformations (SSRIs as a group)</td>
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<td><strong>Statistically significant association with:</strong></td>
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<td></td>
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<td>1) Respiratory distress</td>
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<td></td>
<td></td>
<td>2) Neonatal/infant death within first year of life</td>
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<td></td>
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<td>3) Major congenital malformations (SSRIs – paroxetine and fluoxetine)</td>
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<td>4) Cardiac malformations (SSRI – paroxetine)</td>
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<td></td>
<td></td>
<td>5) PPH – SSRI use in late pregnancy</td>
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<td>6) PNAS – SSRI use</td>
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<tr>
<td></td>
<td></td>
<td>7) Child diagnosis of Autism Spectrum Disorder (ASD) – SSRI use</td>
</tr>
<tr>
<td>Man et al., 2015(^{75})</td>
<td>SSRIs</td>
<td><strong>Statistically significant association with:</strong></td>
</tr>
<tr>
<td>((N=107,688; 4<del>studies</del> included))</td>
<td></td>
<td>1) Low birth weight</td>
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<td></td>
<td></td>
<td>2) Preterm birth</td>
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</tbody>
</table>

**Notes.** \(^1\)Due to limitations in the literature, ‘untreated depression’ refers to depression that is not being treated with medication
<table>
<thead>
<tr>
<th>Meta-analysis</th>
<th>Exposure(^1)</th>
<th>Impact on fetus/child</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kobayashi et al., 2016(^{62})</td>
<td>SSRIs (with comparison groups of other antidepressants and maternal diagnosis of psychiatric illness)</td>
<td><strong>Statistically significant association with:</strong> Child diagnosis of ASD However, no difference in ASD risk between SSRI-exposed and antidepressant-exposed, and no difference in ASD risk between SSRI-exposed women with a psychiatric illness and SSRI-unexposed women with a psychiatric illness.</td>
</tr>
<tr>
<td>Eke et al., 2016(^{76})</td>
<td>SSRIs</td>
<td><strong>Statistically significant association with:</strong> 1) Preterm birth 2) Lower birth weight 3) Respiratory distress syndrome</td>
</tr>
<tr>
<td>Kaplan et al., 2016(^{64})</td>
<td>SSRIs</td>
<td><strong>Statistically significant association with:</strong> Child diagnosis of ASD</td>
</tr>
<tr>
<td>Brown et al., 2017(^{63})</td>
<td>SSRIs</td>
<td><strong>Statistically significant association with:</strong> Child diagnosis of ASD However, in analyses restricted to participants with maternal mental illness (exposed versus unexposed to SSRIs), there was no difference in ASD risk. Increased ASD risk was completely attenuated in all analyses that adjusted for maternal mental illness, with the exception of the maternal mental illness-adjusted meta-analysis of 4 case-control studies that continued to show a significant association with ASD for first trimester SSRI exposure.</td>
</tr>
<tr>
<td>Kaplan et al., 2017(^{65})</td>
<td>SSRIs; Untreated depression</td>
<td><strong>Statistically significant association (for both SSRIs and untreated depression) with:</strong> Child diagnosis of ASD</td>
</tr>
<tr>
<td>Andalib et al., 2017(^{77})</td>
<td>SSRIs</td>
<td><strong>Statistically significant association with:</strong> Child diagnosis of ASD</td>
</tr>
</tbody>
</table>

Notes. \(^1\)Due to limitations in the literature, ‘untreated depression’ refers to depression that is not being treated with medication
<table>
<thead>
<tr>
<th>Meta-analysis</th>
<th>Exposure</th>
<th>Impact on fetus/child</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zwink &amp; Jenetzky, 2018&lt;sup&gt;78&lt;/sup&gt; (N=5,687,180; 9 studies included)</td>
<td>Antidepressants</td>
<td>No significant association with: Anorectal malformations (antidepressants as a whole, or SSRIs)</td>
</tr>
<tr>
<td>Gao et al., 2018&lt;sup&gt;60&lt;/sup&gt; (N=9,088,145; 29 studies included)</td>
<td>SSRIs</td>
<td>No significant association with: Congenital malformations – Fluvoxamine</td>
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<tr>
<td></td>
<td></td>
<td>Statistically significant association with:</td>
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<tr>
<td></td>
<td></td>
<td>1) Major congenital malformations – SSRIs as a group; Paroxetine, Fluoxetine, Sertraline, Citalopram, Escitalopram</td>
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<tr>
<td></td>
<td></td>
<td>2) Cardiac defects (SSRI use in first trimester)</td>
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<tr>
<td></td>
<td></td>
<td>a. Septal defects</td>
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<tr>
<td></td>
<td></td>
<td>b. Atrial septal defects</td>
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<td></td>
<td></td>
<td>c. Right ventricular outflow tract defects</td>
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<td></td>
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<td>3) Neural tube defects (SSRI use in first trimester)</td>
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<td>4) Cystic kidney disease (SSRI use in first trimester)</td>
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<td>5) Clubfoot (SSRI use in first trimester)</td>
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<td></td>
<td>6) Abdominal wall defects (omphalocele, gastroschisis; SSRI use in first trimester)</td>
</tr>
<tr>
<td>Masarwa et al., 2019&lt;sup&gt;61&lt;/sup&gt; (N=7,080,850; 11 studies included)</td>
<td>SSRIs/SNRIs</td>
<td>Statistically significant association with: PPH (Most studies (7/11) only included data on SSRIs)</td>
</tr>
<tr>
<td>Ng et al., 2019&lt;sup&gt;79&lt;/sup&gt; (N=7,515,051; 8 studies included)</td>
<td>SSRIs</td>
<td>Statistically significant association with: PPH</td>
</tr>
</tbody>
</table>

Notes. ¹Due to limitations in the literature, ‘untreated depression’ refers to depression that is not being treated with medication
Table 1.2. Summary of meta-analyses evaluating impact of depression- and treatment-related exposures during pregnancy on the fetus/child – grouped by exposure

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Outcome - No statistically significant association</th>
<th>Outcome - Statistically significant association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Untreated depression</td>
<td><strong>1) Birth weight^</strong></td>
<td>1) Less frequent breastfeeding initiation</td>
</tr>
<tr>
<td></td>
<td>2) Neonatal intensive care unit admissions</td>
<td>2) <strong>Preterm delivery</strong>*</td>
</tr>
<tr>
<td></td>
<td>3) Preeclampsia</td>
<td>3) <strong>Lower birth weight^</strong></td>
</tr>
<tr>
<td></td>
<td>4) APGAR scores</td>
<td>4) Child diagnosis of Autism Spectrum Disorder</td>
</tr>
<tr>
<td></td>
<td>5) Gestational age at delivery (mean difference)</td>
<td></td>
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<tr>
<td></td>
<td>6) Intrauterine growth restriction</td>
<td></td>
</tr>
<tr>
<td>Antidepressants - overall</td>
<td><strong>1) Neonatal convulsions</strong></td>
<td><strong>1) Low birth weight</strong>*</td>
</tr>
<tr>
<td></td>
<td>2) <strong>Preterm birth^</strong></td>
<td>2) <strong>Preterm birth^</strong></td>
</tr>
<tr>
<td></td>
<td>3) Breastfeeding outcomes</td>
<td>3) Lower gestational age at delivery</td>
</tr>
<tr>
<td></td>
<td>4) Fetal growth</td>
<td>4) Lower APGAR scores</td>
</tr>
<tr>
<td></td>
<td>5) Miscarriage</td>
<td>5) Cardiac malformations</td>
</tr>
<tr>
<td></td>
<td>6) Congenital malformations – general</td>
<td>a. Septal heart defects</td>
</tr>
<tr>
<td></td>
<td>7) Anorectal malformations</td>
<td>b. <strong>Respiratory distress</strong>*</td>
</tr>
<tr>
<td></td>
<td>8) Major congenital malformations</td>
<td>c. Tremors</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6) Poor neonatal adaptation syndrome (PNAS)</td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td>SSRIs</td>
<td><strong>1) Major congenital malformations</strong></td>
<td><strong>1) PPH more frequent when SSRIs taken in “late pregnancy”</strong>*</td>
</tr>
<tr>
<td></td>
<td>2) <strong>Cardiac malformations^</strong></td>
<td>2) <strong>Poor neonatal adaptation syndrome (PNAS)^</strong></td>
</tr>
<tr>
<td></td>
<td>3) Anorectal malformations</td>
<td>3) Preterm delivery</td>
</tr>
<tr>
<td></td>
<td>4) Persistent pulmonary hypertension (PPH) when SSRIs taken in ‘early pregnancy’ (~ &lt; 20 weeks)</td>
<td>4) Lower birth weight</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5) Child diagnosis of Autism Spectrum Disorder</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6) <strong>Major congenital malformations^</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>7) <strong>Cardiac malformations^</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>8) Neural tube defects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>9) Cystic kidney disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10) Clubfoot</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11) Abdominal wall defects (including omphalocele and gastroschisis)</td>
</tr>
</tbody>
</table>

Notes. * Found in two meta-analyses; ** Found in three or more meta-analyses; ^ Contradictory findings
<table>
<thead>
<tr>
<th>Exposure</th>
<th>Outcome - No statistically significant association</th>
<th>Outcome - Statistically significant association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine</td>
<td></td>
<td>1) Major congenital malformations**</td>
</tr>
<tr>
<td>Paroxetine</td>
<td></td>
<td>1) Cardiovascular malformations**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2) Major congenital malformations**</td>
</tr>
<tr>
<td>Citalopram / Escitalopram / Sertraline</td>
<td>1) Congenital malformations^</td>
<td>1) Congenital malformations^</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>1) Congenital malformations</td>
<td></td>
</tr>
</tbody>
</table>

*Notes.* *Found in two meta-analyses;** *Found in three or more meta-analyses;* ^Contradictory findings
Treatment decision-making theories

Decision-making theories shed light on many aspects of how individuals make decisions, including in the health care context. It is generally agreed that individuals rely on two systems when making decisions: one that is more unconscious or “automatic”, and one that is more conscious or “controlled”. The majority of DM theories have been developed by men (e.g., von Neumann & Morgenstern’s Utility Theory, Janis & Mann’s Conflict Model of Decision Making, Rosenstock’s Health Belief Model, Rogers’ Protection Motivation Theory, Bandura’s Social Cognitive Theory, Ajzen’s Theory of Planned Behaviour, Kahneman & Tversky’s Prospect Theory) and, historically, have focused on DM as a “rational”, cognitive process, largely neglecting the role of emotion in DM. In contrast, the Wittmann-Price Theory of Emancipated Decision Making in Women’s Healthcare (TEDMWH) was developed by a woman, with a focus on women’s DM regarding health care. The Wittman-Price TEDMWH has its roots in Critical Social Theory, Feminist Theory, and Freire’s Emancipatory Educational theory, and characterizes women’s DM as being influenced by three concepts: personal knowledge, awareness of social norms, and a flexible environment. Personal knowledge is “defined as a woman having thought about her choice in relation to what is best for her”; awareness of social norms is “described as a woman’s awareness that society places more value on one option over another”; and a flexible environment is “one that affords a woman the opportunity to enact on her choice without opposition”.

Treatment decision making – Depression

In health care broadly, key steps in a DM process have been reported to include: identifying treatment options; seeking information; weighing risks and benefits of each option;
making a decision; and evaluating the consequences of the decision\textsuperscript{86–89}. A variety of parameters have been found to impact the treatment DM process including: personal beliefs and values about treatment and illness; cost (individual and system levels); awareness of what treatment options are available; institutional barriers (e.g., policies/practices); and the sociocultural environment\textsuperscript{80,90–92}.

In the depression treatment DM literature, studies have very rarely reported sex- or gender-based analyses or data for women separately. Thus, the literature documenting women’s depression treatment DM is very limited. Two of the most frequently identified barriers (for both men and women) in depression treatment DM are: 1) the stigma of depression\textsuperscript{88,90,91,93–99}; and 2) the fear of dependency on antidepressants\textsuperscript{88,91,94–97,99–102}. Both men and women with depression frequently identify a need for information about treatment options, including medication, and expectations regarding the impact of treatment options (e.g., expected time required for efficacy, anticipated treatment duration, side effects)\textsuperscript{88,94,95,97,103,104}. Feeling uninformed in depression treatment DM has been associated with decisional conflict\textsuperscript{87} (i.e., the experience of “simultaneous opposing tendencies within the individual to accept and reject a given course of action.”\textsuperscript{105}(p. 46)). Lacking information about treatment options can lead not only to decisional conflict, which has been associated with distress and negative emotions\textsuperscript{105}, but also to decisional delay\textsuperscript{95}. An integral aspect of the DM process is evaluating the consequences of options\textsuperscript{87,89,106}; without adequate information to inform this evaluation, fear of making a decision that they would later regret (e.g., in light of previously unavailable information) can lead individuals to delay making a decision. However, it’s important to note the research that has characterized the nature of depression treatment DM as dynamic and subject to re-appraisal\textsuperscript{88,94}. For example, for individuals engaging in antidepressant use, the decision is renewed on a daily basis\textsuperscript{96,97,102}. 
Qualitative studies lend further support to, and context in the interpretation of, these findings. Experiences of depression symptoms and treatment contribute to the iterative process of treatment DM. The relationship of stigma to depression treatment DM is a recurrent theme in this body of literature. Resistance to treatment is often rooted in a reluctance to surrender the identity of someone who doesn’t have mental illness: "Many participants viewed antidepressant pills as a concrete sign, invisible once swallowed, that they inhabited a stigmatized role or had taken on an identity marked by shame" (p. 36). As symptoms of depression increase, individuals are forced to confront the possibility that they may need treatment, but resist engaging in treatment DM to protect their self-identity. There is a tipping point, however, when the perception of increasing symptom severity can act as a facilitator of treatment DM by compelling individuals to acknowledge their need for treatment, representing the formation and/or solidification of a necessity belief.

In terms of implementing a depression treatment decision, one quantitative study focusing on the decision to discontinue or restart antidepressants found only two factors that were significantly associated with implementing the treatment plan: setting the intention to implement the decision, and the participant’s belief in their own ability to make change (self-efficacy). Another study showed that simply expressing positive attitudes towards treatment (in this case - psychotherapy) did not predict subsequent engagement in treatment. One study of women’s experiences of deciding to discontinue antidepressant treatment found that women constructed their decision as responsible, and a pivotal aspect of their argument was the absence of a medication necessity belief. Another study (that conflated sex and gender in an analysis of different treatment options received by men and women) found that women were more likely to

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1 This was the language used by the authors in this paper, and reflected the pressure faced by women to justify their decision to discontinue antidepressants against medical advice.
receive psychotherapy alone, while men were more likely to receive antidepressants alone. The one study that conducted a sex- and gender-based analysis related to treatment DM for depression focused on the gender norm of “toughness”, or the expectation to “tough it out”, in relation to the treatment preference to “wait and see” (i.e., not engage in any treatment). While men were more likely to endorse this “toughness” norm, there were also women who endorsed it, and endorsement of this gender norm, whether by men or women, predicted the treatment preference to “wait and see”.

Arguably, these findings reflect manifestations of individuals’ desire for control over their mental health and interpretations of the role of treatment in relation to personal control; a prominent theme in qualitative studies of depression treatment DM. In the above examples, desire for control either increased the likelihood of engaging in treatment (in relation to higher levels of self-efficacy) or decreased the likelihood of engaging in treatment (in relation to the gender norm of toughness). Further examples from the qualitative literature illustrate participants’ desire to either avoid treatment due to concerns that treatment would mask their “real” self, or alternatively, desire to engage in treatment because it would enable them to feel in control of their behaviour and to express their “true” self. Concerns that medication would mask their “real” self often accompanied fear that the damage would be irreversible – that they would be dependent on medication forever. Individuals who took ownership over their treatment DM – as a means to feel in control of their behaviour – were more likely to engage actively in treatment (and continue taking antidepressants, for example), to tolerate side effects from antidepressants, and to interpret improvement in symptoms as a reason to continue treatment. In contrast, individuals who came to engage in treatment for the good of others, and who placed responsibility for the decision on someone else, were more likely to discontinue
treatment (e.g., due to side effects or because their symptoms had improved). The desire to engage in treatment for the good of others was a prominent theme in a qualitative study of women’s experiences of depression treatment DM (one of only two studies specifically investigating women’s depression treatment DM experiences outside of the perinatal period). In this study, women expressed that their motivation to overcome depression came from their obligation to fulfill their social roles, and that engagement in treatment towards this end represented an honorable form of self-sacrifice.

**Treatment decision making – Depression during pregnancy**

Pregnant women using SSRIs face stigma both as a result of their diagnosis and the perception that ‘good mothers’ don’t take medication. As one woman said of her prenatal antidepressant use:

I don’t tell other people because I feel ashamed of it. [...] My mother doesn’t know. I feel like a heroin addict. I feel like I’m doing something secret and bad.

SSRI use during pregnancy falls by 42-80% compared to pre- and post-pregnancy, with those in greatest need (more depression symptoms and less insight) being less likely to use them. Up to 75% of women discontinuing use of antidepressants shortly prior to, or during, pregnancy subsequently experience clinically significant depression symptoms during their pregnancy. There is a dearth of research, however, into how women make the complex decision of whether to take antidepressants during pregnancy.

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2 While the pregnancy experiences of trans men and genderqueer individuals are important and worthy of investigation, they were not the focus of this dissertation, and none of the literature on depression treatment DM in pregnancy reported these perspectives.
Studies evaluating women’s treatment DM for depression in the prenatal context have explored factors associated with: information seeking; decisional conflict; satisfaction with their decision; and engagement in treatment (Table 1.3). Women have cited a lack of high quality information as a barrier to DM about antidepressant use during pregnancy\textsuperscript{112,117}, and a preference to receive this type of information from a health care provider\textsuperscript{114}. Studies have found the following two predictors of high decisional conflict: higher depression scores\textsuperscript{111}, and being of a younger age, which was explained by feeling less informed\textsuperscript{114}. A study evaluating satisfaction with depression treatment decisions in pregnancy found that women with higher satisfaction scores also had higher total scores on the Emancipated Decision-Making scale, and in particular the subscale measuring women’s awareness of their beliefs and values\textsuperscript{85}. In terms of engagement with depression treatment in pregnancy, studies have found many predictors of using antidepressants for treating depression in pregnancy: positive attitudes towards antidepressants, greater insight into illness, and previous antidepressant use\textsuperscript{117}; lower depression scores, lower perception of risk of harm to the fetus due to medication, receiving more reassuring information, and receiving reassuring information first\textsuperscript{118}; higher scores on the Emancipated Decision-Making scale, and its two subscales – awareness of social norms and a non-judgmental environment supporting women’s freedom of choice\textsuperscript{85}; and feeling more adequately informed and clear about their values\textsuperscript{112}. One study asked participants their reason(s) for stopping their antidepressant for pregnancy\textsuperscript{123}, and found the most frequent response to be the perceived risk of harm to the fetus due to medication, with the next most common responses being: on the advice of a health care professional, and because their symptoms were under control.
Table 1.3. Summary of studies focused on women’s experiences of depression treatment DM for pregnancy

<table>
<thead>
<tr>
<th>Citation, Country</th>
<th>Study Design</th>
<th>Sample (size, characteristics)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bonari et al., 2005&lt;sup&gt;118&lt;/sup&gt;; Canada</td>
<td>Interventional pre-post study</td>
<td>N=300: n=100 women calling about safety of antidepressants; n=100 about antibiotics; n=100 about medications for gastric conditions</td>
</tr>
<tr>
<td></td>
<td>Quantitative with intervention: Questionnaire to assess perceptions of, and DM about, medication use during pregnancy; psychiatric symptoms and treatment assessed</td>
<td>Recruitment: Women calling the Motherisk Program</td>
</tr>
<tr>
<td></td>
<td>Intervention: Evidence-based information provision</td>
<td>Demographics not included</td>
</tr>
<tr>
<td></td>
<td>Follow-up: Call two weeks post-intervention with dichotomous outcome (continued or discontinued medication)</td>
<td>Gestational age at time of recruitment: &lt;6wks</td>
</tr>
<tr>
<td></td>
<td>Analysis: t tests/Wilcoxon signed ranks tests, ANOVA/Kruskal-Wallis tests</td>
<td>Gestational age at time of treatment decision: &lt;8wks</td>
</tr>
<tr>
<td>Bakhireva et al., 2011&lt;sup&gt;124&lt;/sup&gt;; USA</td>
<td>Cross-sectional data from prospective cohort study</td>
<td>N=404: n=181 with medical conditions; n=26 with depression</td>
</tr>
<tr>
<td></td>
<td>Quantitative: Demographics and health questionnaire, including questions about knowledge and attitudes towards medication use in pregnancy; chart review</td>
<td>Recruitment from prenatal clinics</td>
</tr>
<tr>
<td></td>
<td>Analysis: Descriptive statistics, chi-square tests, logistic regression</td>
<td>Majority: Latina (80.5%) immigrant (59.2%) women with low levels of education (68.1%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gestational age at time of recruitment: M=30.7wks; SD=7.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gestational age at time of treatment decision: Not provided</td>
</tr>
<tr>
<td>Patel &amp; Wisner&lt;sup&gt;114&lt;/sup&gt;, 2011; USA</td>
<td>Anonymous, cross-sectional cohort study</td>
<td>N=100: n=27 pregnant; n=73 postpartum (up to 1 year)</td>
</tr>
<tr>
<td></td>
<td>Quantitative: Control Preferences Scale; Problem-Solving DM Scale; Decisional Conflict Scale; questionnaire assessing demographics, health history, depression treatment preferences, and preferences for supports for the treatment DM process</td>
<td>Recruitment: Online, link to survey on five perinatal mood disorders websites</td>
</tr>
<tr>
<td></td>
<td>Analysis: Descriptive statistics, chi-square tests, ANOVA</td>
<td>Majority: Caucasian (96%), married (98%), well-educated (90%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gestational age at time of recruitment- Pregnant group: M=5.6wks; SD=10.4wks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gestational age at time of treatment decision: Not provided</td>
</tr>
</tbody>
</table>

<sup>Note</sup>. wks = weeks
<table>
<thead>
<tr>
<th>Citation, Country</th>
<th>Study Design</th>
<th>Sample (size, characteristics)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mulder et al., 2012; Canada</td>
<td>Retrospective cohort study</td>
<td>$N=94$ (all had taken antidepressants during pregnancy); $n=78$ continued taking antidepressants throughout pregnancy “continuers”; $n=16$ discontinued antidepressants “discontinuers”</td>
</tr>
<tr>
<td></td>
<td>Quantitative: 67-item questionnaire assessing demographics, health history, knowledge and attitudes towards medication use in pregnancy, and the social and emotional experience of taking antidepressants during pregnancy</td>
<td>Recruitment: Women who had called the Motherisk Program or participated in a study of antidepressant use in pregnancy</td>
</tr>
<tr>
<td></td>
<td>Analysis: Descriptive statistics</td>
<td>Majority: Caucasian (88%), married (85%), well-educated (78%)</td>
</tr>
<tr>
<td>Battle et al., 2013; USA</td>
<td>Cross-sectional data from prospective cohort study</td>
<td>$N=61$: $n=31$ with depression; $n=30$ without depression</td>
</tr>
<tr>
<td></td>
<td>Mixed methods</td>
<td>Recruitment in the community</td>
</tr>
<tr>
<td></td>
<td>Quantitative: Decisional Conflict Scale (depressed group only); demographics and health questionnaire; psychiatric symptoms and treatment assessed</td>
<td>Majority: Caucasian (72.1%), in a relationship (67.2%)</td>
</tr>
<tr>
<td></td>
<td>Quantitative analysis: Descriptive statistics, chi-square tests, $t$ tests</td>
<td>Gestational age at time of interview: ~32wks</td>
</tr>
<tr>
<td></td>
<td>Qualitative: Semi-structured interviews (depressed group only)</td>
<td>Gestational age at time of treatment decision: Not provided</td>
</tr>
<tr>
<td></td>
<td>Qualitative analysis: Not identified</td>
<td></td>
</tr>
<tr>
<td>Misri et al., 2013; Canada</td>
<td>Prospective cohort study</td>
<td>$N=50$: $n=30$ taking antidepressants; $n=20$ not taking antidepressants</td>
</tr>
<tr>
<td></td>
<td>Mixed methods</td>
<td>Recruitment: Women receiving care at a tertiary specialty clinic for reproductive mental health</td>
</tr>
<tr>
<td></td>
<td>Quantitative: Psychiatric symptoms and attitude toward treatment assessed every 4 wks between 18-34 wks gestation and at 1 month postpartum</td>
<td>Majority: Caucasian (76.6%), married/common law (83%)</td>
</tr>
<tr>
<td></td>
<td>Quantitative analysis: Descriptive statistics, chi-square tests, $t$ tests, MANOVA, hierarchical linear modeling</td>
<td>Gestational age at time of recruitment: 18 – 34 wks</td>
</tr>
<tr>
<td></td>
<td>Qualitative: One question interview conducted at baseline</td>
<td>Gestational age at time of treatment decision: Not provided</td>
</tr>
<tr>
<td></td>
<td>Qualitative analysis: Not identified</td>
<td></td>
</tr>
</tbody>
</table>

*Notes. wks = weeks*
<table>
<thead>
<tr>
<th>Citation, Country</th>
<th>Study Design</th>
<th>Sample (size, characteristics)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Price &amp; Bentley, 2013; USA</td>
<td>Anonymous, cross-sectional cohort study Mixed methods Questionnaire with open and closed ended questions assessing demographics, health history, perceptions of, and experience with, DM regarding antidepressant treatment during pregnancy or postpartum Quantitative analysis: Descriptive statistics Qualitative analysis: Thematic analysis</td>
<td>N=171: n=83 female patients (n=15 pregnant, n=42 postpartum within the past 2 years, n=26 unspecified); n=88 maternity care providers Recruitment: Online, link to survey on mental health/parenting/prenatal websites Majority of patients: Caucasian (90%), well-educated (94%) Gestational age at time of recruitment: Not provided Gestational age at time of treatment decision: Not provided</td>
</tr>
<tr>
<td>Stepanuk et al., 2013; USA</td>
<td>Anonymous, cross-sectional cohort study Quantitative: Wittmann-Price Revised Emancipated DM Scale(^{125}), Satisfaction with Decision Scale; demographics questionnaire including questions about history of mental illness and treatment decision during pregnancy Analysis: Descriptive statistics, (t) tests, multiple regression</td>
<td>N=143: n=42 who chose not to start/continue antidepressants; n=72 who chose to start/continue antidepressants as prescribed; n=29 other (including taking antidepressants but not as prescribed) Recruitment: Online, link to survey on pregnancy-related websites Majority: Caucasian (95%), well-educated (89%), living with the co-parent of the baby (91.5%) Gestational age at time of recruitment: (M=22)wks; (SD=10)wks Gestational age at time of treatment decision: (M=8)wks; (SD=7)wks</td>
</tr>
</tbody>
</table>

Notes. wks = weeks
<table>
<thead>
<tr>
<th>Citation, Country</th>
<th>Study Design</th>
<th>Sample (size, characteristics)</th>
</tr>
</thead>
</table>
| Walton et al., 2014; Canada | Cross-sectional cohort study  
Mixed methods  
Quantitative: Baseline- Decisional Conflict Scale; demographics and health questionnaire; psychiatric symptoms and treatment assessed; chart review  
Quantitative analysis: Descriptive statistics, chi-square tests, $t$ tests  
Those with moderate-high scores on decisional conflict scale invited for qualitative interview  
Qualitative: Semi-structured interviews with 5 women taking antidepressants and 5 women not taking antidepressants  
Qualitative analysis: Thematic analysis | $N=40$: $n=21$ taking antidepressants; $n=19$ not taking antidepressants  
Recruitment: Women receiving care at a tertiary specialty clinic for reproductive mental health  
Majority: Married/common law (80%), well-educated (82.5%), high household income (56.4%) (ethnicity not included)  
Gestational age at time of recruitment: $M=25.4$ wks; $SD=9.06$ wks  
Gestational age at time of treatment decision: Not provided |
| Nygaard et al., 2015; Denmark | Cross-sectional cohort study with follow-up member checking  
Qualitative: Semi-structured interviews conducted during the third trimester of pregnancy  
Analysis: Constructivist grounded theory | $N=8$ women, 11 interviews  
Recruitment: Women receiving care from midwives  
Majority: Caucasian (100%), in a relationship (87.5%)  
Gestational age at time of interview: $3^{rd}$ trimester  
Gestational age at time of treatment decision: Preconception, decision revisited in $1^{st}$ trimester, with 2/8 participants changing their decision |

*Notes. wks = weeks*
<table>
<thead>
<tr>
<th>Citation, Country</th>
<th>Study Design</th>
<th>Sample (size, characteristics)</th>
</tr>
</thead>
</table>
| Kothari et al., 2019; Australia | Cross-sectional cohort study  
Quantitative: Questionnaire to assess perceptions of, and DM about, medication use during pregnancy; psychiatric history and treatment assessed  
Quantitative analysis: Descriptive statistics, chi-square tests, t tests | $N=503; n=47$ (9.3%) women taking antidepressant/anxiolytic medications at the beginning of, or immediately before, their current pregnancy  
Recruitment: Women attending their first antenatal obstetrician appointment at a tertiary hospital  
Majority: Age 21 – 35 (81%), in their first or second pregnancy (62%)  
Gestational age at time of recruitment: ~20wks  
Gestational age at time of treatment decision: Not provided |

Notes. wks = weeks
Qualitative research into depression treatment DM in the context of pregnancy has identified quite a lot of overlap with themes found for depression treatment DM outside the context of pregnancy, but also some unique elements. Firstly, women feel a great deal of pressure to conform to societal norms during pregnancy, and experience guilt if they perceive themselves to be violating the norms of ‘good motherhood’ (e.g., by taking medication during pregnancy)\textsuperscript{110–112,115}. It is perhaps for this reason that women particularly desire a non-judgmental environment that supports their freedom of choice\textsuperscript{85,113}. Secondly, evaluating the consequences of options is central to depression treatment DM generally, but during pregnancy the complexity of this evaluation multiplies because women are evaluating consequences of treatment options not only for themselves, but also for their fetuses. Most often, this evaluation triggers fear of causing harm to the fetus\textsuperscript{113,117} – either as a result of taking antidepressants or due to untreated depression – and women report feeling like they have to make a trade-off between their own health and their baby’s health\textsuperscript{110–112}. Thus, women could greatly benefit from more information about the chance that antidepressants will alleviate/prevent their symptoms at a given dose as they negotiate this evaluation process during DM about taking antidepressants during pregnancy. Pharmacogenetic testing is a possible source of such insight into the efficacy of antidepressants at particular doses.

**Pharmacogenetic testing to predict SSRI response**

SSRI metabolism is driven by estrogen sensitive enzymes\textsuperscript{126} including two in the cytochrome P450 family: CYP2C19 and CYP2D6. These enzymes, encoded by genes of the same names, act to metabolize many drugs, including SSRIs. CYP2D6 is primarily responsible for metabolizing the SSRIs paroxetine and fluvoxamine, and CYP2C19 is primarily responsible for metabolizing the SSRIs citalopram, escitalopram and sertraline. In the genes encoding these
enzymes, the six most common genetic variants (also known as alleles) that are known to decrease enzyme activity or production are \textit{CYP2D6*3}, \textit{*4}, \textit{*5}, and \textit{*6}, and \textit{CYP2C19*2}, and \textit{*3}. These variants cause “slow” or “poor” metabolism, whereby a drug accumulates faster than it can be broken down, increasing susceptibility to side effects and drug discontinuation\textsuperscript{127}. The three most common variants in these genes that are known to increase enzyme activity or production are \textit{CYP2D6*1xN} and \textit{*2xN}, and \textit{CYP2C19*17}. These variants cause “fast” metabolism, whereby a drug breaks down more quickly, leaving inadequate levels for symptom control.

It follows, then, that alleles associated with slow or fast metabolism - low efficacy alleles - should impact effective SSRI dosages, and that ignoring these factors puts patients at risk of improper dosing, and sub-optimal treatment. Frequencies of these low efficacy alleles vary by ethnicity. However, there are no differences in their frequency between general populations and populations taking SSRIs\textsuperscript{128-132}, within an ethnic group. The average population frequency for low efficacy alleles for Caucasian and Asian populations (combined) is 37\%\textsuperscript{128,129}. Importantly, functionality of these alleles is consistent across populations\textsuperscript{128,129}.

The Clinical Pharmacogenetics Implementation Consortium (CPIC) and the Dutch Pharmacogenetics Working Group (DPWG) are the two foremost organizations worldwide dedicated to developing pharmacogenetic clinical practice guidelines. The 2015 CPIC pharmacogenetic clinical practice guideline included the drugs paroxetine, fluvoxamine, citalopram, escitalopram, and sertraline in relation to \textit{CYP2D6} and/or \textit{CYP2C19} genotypes\textsuperscript{133}. The 2018 DPWG pharmacogenetic clinical practice guideline included the drugs paroxetine, fluoxetine, fluvoxamine, citalopram, escitalopram, and sertraline in relation to \textit{CYP2D6} and/or \textit{CYP2C19} genotypes\textsuperscript{134}. Recommendations from the two organizations are presented in Table
1.4. Both CPIC and DPWG agree that there are insufficient data regarding the impact of CYP450 alleles on either pharmacokinetic or therapeutic outcomes for fluoxetine; no pharmacogenetic recommendations have yet been made for fluoxetine therapy.
**Table 1.4.** Summary of dosing recommendations by the organizations CPIC and DPWG by genotype (*CYP2D6* and *CYP2C19*) for the SSRIs citalopram, escitalopram, fluvoxamine, paroxetine, and sertraline

<table>
<thead>
<tr>
<th>Organization</th>
<th>Citalopram/escitalopram</th>
<th>Fluvoxamine</th>
<th>Paroxetine</th>
<th>Sertraline</th>
</tr>
</thead>
<tbody>
<tr>
<td>**CYP2D6 - Poor metabolizer (carriers of two copies of <em>CYP2D6</em> *3, *4, <em>5, or <em>6)</em></em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPIC</td>
<td>Avoid (select alternative) OR Start at 25-50% of usual starting dose and titrate to response</td>
<td>Avoid (select alternative) OR Start at 50% of usual starting dose and titrate to response</td>
<td>None - Insufficient evidence</td>
<td>None - Insufficient evidence</td>
</tr>
<tr>
<td>DPWG</td>
<td>None - Insufficient evidence</td>
<td>None - Insufficient evidence</td>
<td>No change necessary</td>
<td>None - Insufficient evidence</td>
</tr>
<tr>
<td>**CYP2D6 - Ultra-rapid metabolizer (carriers of <em>CYP2D6</em> <em>1xN or <em>2xN)</em></em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPIC</td>
<td>None - Insufficient evidence</td>
<td>None - Insufficient evidence</td>
<td>Avoid (select alternative)</td>
<td>None - Insufficient evidence</td>
</tr>
<tr>
<td>DPWG</td>
<td>None - Insufficient evidence</td>
<td>None - Insufficient evidence</td>
<td>Avoid (select alternative)</td>
<td>None - Insufficient evidence</td>
</tr>
</tbody>
</table>

*Notes.* Cells in dark gray are not addressed in the relevant guidelines. Red font = inconsistent recommendations between organizations.
<table>
<thead>
<tr>
<th>Organization</th>
<th>Citalopram/escitalopram</th>
<th>Fluvoxamine</th>
<th>Paroxetine</th>
<th>Sertraline</th>
</tr>
</thead>
<tbody>
<tr>
<td>**CYP2C19 - Poor metabolizer (carriers of two copies of CYP2C19<em>2 or <em>3)</em></em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPIC</td>
<td>Avoid (select alternative) OR Start at 50% of usual starting dose and titrate to response</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DPWG</td>
<td>Escitalopram max daily dose: Adults up to 65 years: 10mg Adults 65 years or older: 5mg Citalopram max daily dose: Adults up to 65 years: 20mg (tablets) or 16mg (drops) Adults 65 years or older: 10mg (tablets) or 8mg (drops)</td>
<td>None - Insufficient evidence</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

*Notes.* Cells in dark gray are not addressed in the relevant guidelines. Red font = inconsistent recommendations between organizations.
<table>
<thead>
<tr>
<th>Organization</th>
<th>Citalopram/escitalopram</th>
<th>Fluvoxamine</th>
<th>Paroxetine</th>
<th>Sertraline</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPIC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DPWG</td>
<td>Escitalopram max daily dose:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adults up to 65 years: 15mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adults 65 years or older: 7.5mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Citalopram max daily dose:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adults up to 65 years: 30mg (tablets) or 22mg (drops)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adults 65 years or older: 15mg (tablets) or 10mg (drops)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CYP2C19 - Intermediate metabolizer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPIC</td>
<td>Avoid (select alternative)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DPWG</td>
<td>Escitalopram:</td>
<td>None - Insufficient evidence</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avoid (select alternative)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Citalopram:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No change necessary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Less evidence of a negative impact on sertraline metabolism, but if patients are not responding to the recommended maintenance dose of sertraline, consider switching to an alternative SSRI (e.g., paroxetine)</td>
<td></td>
<td>No change necessary</td>
<td></td>
</tr>
</tbody>
</table>

Notes. Cells in dark gray are not addressed in the relevant guidelines. Red font = inconsistent recommendations between organizations. ¹The guidelines note that there may be a clinically significant difference in therapeutic response between patients who carry only one *17 allele compared to patients who carry two *17 alleles.
Discrepancies between these recommendations could be a factor contributing to the lack of integration of pharmacogenomic testing into clinical practice to date\textsuperscript{135,136}. Fortunately, the organizations CPIC and DPWG have expressed their commitment to harmonizing the recommendations in their guidelines as a step towards facilitating clinical implementation of pharmacogenomic testing worldwide\textsuperscript{137}.

**Pharmacogenetic variants and SSRI response in pregnancy**

In pregnancy, the activity of CYP2D6 increases by 50-200%\textsuperscript{138,139}, while CYP2C19 decreases by \textasciitilde50\%\textsuperscript{140}, particularly in the third trimester. Though higher SSRI doses are generally required in late pregnancy to achieve pre-pregnancy serum concentrations\textsuperscript{141–143}, the effect of genotype in pregnancy is largely unknown. It has been explored in only one study, which found a differential effect of paroxetine based on CYP2D6 genotype; plasma drug concentrations decreased and depression symptoms increased in “fast metabolizers”, while plasma drug concentrations increased and depression symptoms stabilized in “slow metabolizers”\textsuperscript{132}.

**Gaps in the literature**

Though women find DM about prenatal SSRI use challenging\textsuperscript{112,144}, there are limited data about how women make these decisions or how to best support their DM. Though depression symptoms have been observed to peak in the second or third trimesters\textsuperscript{44,145}, the only studies of prenatal depression treatment DM that reported gestational age at the time of DM were of DM that occurred in the first trimester\textsuperscript{85,110,114,118}. Only one study has examined the effect of paroxetine by genotype in pregnant women\textsuperscript{132}, and there have been no studies published of the
effect of other SSRIs by genotype in pregnant women. Thus, though CPIC and DPWG guidelines recommend prescribing changes for paroxetine, citalopram, escitalopram, and sertraline in response to \textit{CYP2D6} and \textit{CYP2C19} genotypes\textsuperscript{133,134}, these recommendations do not differentiate based on sex or address pregnancy - so, whether they effectively apply in this population is unknown.
Chapter 2: A constructivist, women-centred decision-making grounded theory for antidepressant use in pregnancy
Purpose

The purpose of this study was to develop a constructivist grounded theory, within a feminist theoretical framework, of women’s perinatal depression treatment decision making.

Methods

We used constructivist grounded theory, within a feminist theoretical framework, to develop a DM theory for prenatal SSRI use informed by women’s experiences, beliefs, and values. Feminist theory is ideal for working with a stigmatized group of women given its focus on validating women’s perspectives. Grounded theory is an established methodology for gathering in-depth data to understand social processes. These theories emphasize centering the human experience in knowledge creation; applying them together amplifies women’s voices within the co-created DM theory.

Feminist theoretical framework

Feminism typically assumes plurality in the experiences of women, and acknowledges the intersectional aspects of women’s identities and lives. Further, feminism(s) recognize the historical and contemporary mechanisms of oppressing women that act across systemic and individual levels, and share a foundational goal of creating social change to redress this imbalance. Research guided by feminist theory privileges women’s knowledge and emotions, and the validity of women’s perspectives. Research procedures within a feminist framework emphasize minimizing the power differential between researcher and participant, and encourage the researcher to empower participants to take ownership in the research process.
**Grounded theory**

Grounded theory was first articulated as a research method by Barney Glaser and Anselm Strauss in their 1967 text *The Discovery of Grounded Theory*, in which they described grounded theory as “the discovery of theory from data”\(^1\). Such theory generation was deemed to be of value because of its power to predict or explain social phenomena. Glaser and Strauss emphasized an empirical method that privileged staying close to the data, with an analytic process that involved theoretical sampling, constant comparison of data, and responsiveness to data collection and the “emerging” theory. More specifically, the grounded theory method starts with purposive sampling and line-by-line coding. Coding builds a bridge between the data and the theory; it is a tool by which abstraction is achieved. The constant comparative method uses codes in comparing and contrasting each piece of data iteratively. Through this analytic process, theoretical links are established between categories and themes, and tested against new pieces of data. Data collection and analysis thus occur concurrently, with refinements made to the data collection process (e.g., the interview guide) as needed. Gradually, codes are built into categories, and sampling shifts from purposive to theoretical. Theoretical sampling is responsive to the constant comparison process, and aims to enrich the theory under development through the elaboration of concepts and focused interrogation of dimensions of the theory\(^2\). Ultimately, through this iterative process, categories are connected in a cohesive theoretical model. Another fundamental tenet of grounded theory described by Glaser and Strauss was “theoretical saturation”, defined as occurring when “no additional data are being found whereby the sociologist can develop properties of the category”\(^2\). This is thus the criterion used to determine when data collection is complete and the theory most likely to be useful. They noted the importance of attempting to collect data from sources with significantly different
characteristics when evaluating whether the theory has reached saturation – such that the theory will have the widest applicability.

Subsequently, a rift developed between Glaser and Strauss, and each continued publishing and developing different versions of grounded theory. Particularly well known is the 1990 text *Basics of qualitative research: Grounded theory procedures and techniques* by Strauss and Corbin. This book gained popularity because it aimed to break down grounded theory into concrete steps to support trainees in its implementation. In this articulation of grounded theory, Strauss and Corbin focused on one technique for theoretical coding called “axial coding”. They provided structure around how to perform axial coding through the elaboration of a “coding paradigm” and “conditional matrix”; tools which provide a framework that researchers can use to interrogate the context around the phenomenon under study and, in so doing, enrich their analyses. The definition of theoretical saturation in this text is very similar to the definition proposed in the original grounded theory text by Glaser and Strauss, with slight modifications to embrace an emphasis on axial coding.

More recently, Kathy Charmaz identified a lack of ontological and epistemological clarity within both Glaser’s and Strauss’ formulations of grounded theory, but that elements of positivism or post-positivism seemed to underpin their descriptions of how to use the grounded theory method. For example, the “emergence” of theory from data implied an external reality that revealed itself to the researcher. Charmaz put forward a social constructionist articulation of grounded theory that explicitly claimed a constructivist paradigmatic orientation and the researcher as an active participant involved in creating the theory. The way Charmaz discussed her approach to grounded theory resonated strongly with my values as a researcher and my beliefs that one’s ability to know the multiple realities of human experiences is inseparable from
how one sees the world. Thus, I chose to use the constructivist grounded theory method, as described by Charmaz.

Further, I did not seek theoretical saturation, but rather theoretical “sufficiency”\(^{154}(p. 117)\). As has been previously discussed, it is common for authors to claim saturation without justifying this claim, or providing detail regarding how saturation was achieved\(^{155–157}\). In response, many authors have advocated for researchers to specify their approach to evaluating saturation within their study, and some have proposed specific approaches for evaluation\(^{158,159}\). Mason\(^{2010}\) highlighted the likelihood that pragmatic factors often play a major role in determining the point at which “saturation” has been reached\(^{160}\). As I reflected on these expositions regarding saturation, it felt to me that paradigmatic orientation was inadequately addressed. Saturation feels to me to have positivist undertones, and to relate to how well the developed theory reflects an external reality. From a constructivist stance, it is always possible to continue theory construction and further develop characteristics of the theory through the involvement of additional realities. Striving instead for theoretical sufficiency offers a pragmatic approach with a more overt and direct connection to the goals of the research; the researcher asks themselves whether the theory they have created is adequate in terms of the use for it that they envisioned.

**Recruitment and theory co-creation**

Women were recruited from the BC RMH Program, the BC psychiatric genetic counselling (Adapt) clinic, or through community advertising (online and posters/bookmarks). In keeping with standard qualitative practice, we used purposive sampling\(^2,161\), with selection based on factors that may affect the DM process (most importantly, the outcome of the DM process – whether or not women had decided to take antidepressants during pregnancy) to maximize the diversity of perspectives included in the developing theory. Eligibility criteria included: 1) a
history of depression, 2) pregnant or planning a pregnancy, 3) had decided, or was deciding, about taking antidepressants during pregnancy, and 4) English-speaking. Exclusion criteria included: 1) under age 19 (BC age of majority), and 2) clinician/researcher judgement that patient’s psychiatric symptoms would compromise their ability to provide informed consent (e.g., actively psychotic/actively suicidal) or that participation could be detrimental. Clinicians at the RMH and Adapt clinics asked eligible women if they would be interested in hearing more about the research opportunity. Contact information provided by those that were interested was then provided to the lead investigator (CH), who conducted the informed consent process. The study was approved by the UBC/Children’s and Women’s Hospital ethics board (H15-01687).

Women who provided written informed consent then completed a brief demographics questionnaire (Appendix I), administered using REDCap (tools and data storage hosted securely at BC Children’s Hospital). The demographics questionnaire included questions to confirm eligibility, such as “have you ever experienced depression?”. Consistent with the feminist framework, CH invited participants to choose their own pseudonym for the research or to empower the researcher to select a pseudonym. CH then conducted semi-structured interviews by phone or in person (N=31). Questions in the initial interview guide (Appendix II) were informed by sensitizing concepts from the literature (page 16), and the clinical and personal experiences of the research team. Interviewing was responsive to priorities identified by participants with respect to the research topic, consistent with both the feminist framework and constructivist grounded theory methods. Further, CH engaged in reciprocal self-disclosure (also consistent with a feminist framework) following two guiding principles: 1) participants asked directly about her experience; and 2) CH judged that the disclosure would support participants to engage openly in the interview, and that her own motivation for sharing was in the interests of
the participant, rather than her own interests. All participants were asked after the interview for consent to re-contact regarding any points requiring clarification, and whether they would like to receive a summary of the study findings. Interviews were digitally recorded and transcribed verbatim, with the exception of one interview. This participant was not comfortable with the recorder, but agreed that the interviewer could take notes throughout the interview. Transcription was provided by the Canadian transcription service “Transcript Heroes”, or volunteers working with the Translational Psychiatric Genetics Group (one transcribing, a second checking the transcript against the recording). CH read through all transcripts in their entirety, making edits as needed for medical terminology, slang, or abbreviations, and reviewed the audio recordings for time-stamped sections of transcripts that were unintelligible to the transcriptionist. The recorder failed part-way through one interview; in this case, CH wrote notes from memory immediately after the conclusion of the interview for the section of the interview that was not recorded, and then asked the participant to check the full transcript for consistency with the participant’s experiences. The participant confirmed that the transcript was an accurate representation of her experience.

Line-by-line coding of initial interviews was used to generate a preliminary coding framework. LB provided expert audit of this coding framework, and worked closely with CH to refine codes and the developing theory throughout analysis. Additionally, CH maintained a reflexive journal, wrote memos, regularly engaged in peer debriefing, and paid attention to disconfirmatory evidence. Once a first draft of the theory was created, a 5-page document summarizing the theoretical model, with illustrative quotes, was prepared to share with participants interested in a follow-up feedback interview (Appendices III & IV). CH conducted participant feedback follow-up interviews with approximately 1/5th of participants ($n=6$; 2 who
had chosen to take antidepressants at the time of the initial interview, 2 who had chosen not to take antidepressants, and 2 who were undecided). All participants invited for a feedback interview agreed to participate. The summary document was shared with participants in advance (all preferred to receive it by email). These interviews were by phone or in person, and occurred between 1 – 3 years following initial interviews. Data management and analysis were supported by NVivo version 12.

Results

Interviews were conducted with 31 participants, at various stages of DM (see Table 2.1). Interviews ranged from 37 – 130 minutes (M=73 minutes), totaling 2264 minutes (37.7 hours), which were transcribed into 1280 pages of text. There were 14 participants taking antidepressants during pregnancy, or planning to do so, at the time of interview, 11 participants who were not taking antidepressants during pregnancy, and 6 participants who were undecided (all of whom were preconception). There were a minority of participants (n=4) whose decision about taking antidepressants during pregnancy changed over the perinatal period. Three participants initially planned not to take antidepressants during pregnancy, but ended up taking them after unsuccessful preconception physical experiments (page 98). One participant started taking antidepressants in the third trimester, after the onset of an episode of depression.

Participant characteristics

Participants were not asked to identify their sex or gender, however, all participants self-identified as ‘women’ (in response to the recruitment/consent materials) and so that will be used to describe all participants. Participants ranged in age from 25 – 43 years (M=33 years). The majority of participants were pregnant (74.2%; gestational age range: 4 – 39.29 weeks, M=30
weeks), expecting their first child (61%), and in a committed relationship (93.5%) (Table 2.2). Most of the women in this study had over a decade of experience managing their mental health since their first recognized episode of depression (range: 3 – 25 years; $M=12$ years). All women in this study had access to stable housing and interacted with the healthcare system to a greater or lesser extent.
Table 2.1. Decisions made by participants regarding the use of antidepressants during pregnancy at different stages of the perinatal period, as reported in the one prenatal interview [- = not applicable at time of interview; for example, women interviewed during the first trimester could not yet report on decisions made later in the pregnancy].

<table>
<thead>
<tr>
<th>Pseudonym</th>
<th>Preconception</th>
<th>1st Trimester</th>
<th>2nd Trimester</th>
<th>3rd Trimester</th>
<th>Decision status at time of interview</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rebecca</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>-</td>
<td>Yes</td>
</tr>
<tr>
<td>Twyla</td>
<td>Yes; ↓</td>
<td>Yes</td>
<td>-</td>
<td>-</td>
<td>Yes</td>
</tr>
<tr>
<td>Jane</td>
<td>Yes; ↓</td>
<td>↑</td>
<td>↑</td>
<td>-</td>
<td>Yes</td>
</tr>
<tr>
<td>Carolyn</td>
<td>Yes</td>
<td>Yes</td>
<td>↑</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Sarah</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>-</td>
<td>Yes</td>
</tr>
<tr>
<td>Nadia</td>
<td>No; ↓, Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>↑</td>
<td>Yes</td>
</tr>
<tr>
<td>Hazel¹</td>
<td>Yes; ↓, †</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Farha</td>
<td>Undecided; ↓</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Undecided</td>
</tr>
<tr>
<td>Samantha</td>
<td>Yes; †</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Yes</td>
</tr>
<tr>
<td>Whitney</td>
<td>No; ↓, Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Notes. ↓ = attempted to decrease dose; ↓ = decreased dose; ↑ = increased dose; † = stopped medication; †† = switched medication; - = not applicable at time of interview; bold = change in decision. ¹Hazel was taking multiple antidepressants preconception. She decided to continue taking some at a lower dose, but decreased the dose for those, and stopped others.
<table>
<thead>
<tr>
<th>Pseudonym</th>
<th>Preconception</th>
<th>1&lt;sup&gt;st&lt;/sup&gt; Trimester</th>
<th>2&lt;sup&gt;nd&lt;/sup&gt; Trimester</th>
<th>3&lt;sup&gt;rd&lt;/sup&gt; Trimester</th>
<th>Decision status at time of interview</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elizabeth</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>-</td>
<td>No</td>
</tr>
<tr>
<td>Stacy</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Gail</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Molly</td>
<td>No; ↓, Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Stephanie</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Desiree</td>
<td>Undecided; ↓</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Undecided</td>
</tr>
<tr>
<td>Sherry</td>
<td>Yes</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Yes</td>
</tr>
<tr>
<td>Lena</td>
<td>Undecided; ↓</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Undecided</td>
</tr>
<tr>
<td>Audrey</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Natsumi</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>-</td>
<td>No</td>
</tr>
<tr>
<td>Sierra&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No; ↓</td>
<td>No; ●</td>
<td>No</td>
<td>-</td>
<td>No</td>
</tr>
<tr>
<td>Linda</td>
<td>N/A (unplanned)</td>
<td>No; ●</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Notes. ↓ = attempted to decrease dose; ↓ = decreased dose; ↑ = increased dose; ● = stopped medication; → = switched medication; - = not applicable at time of interview; bold = change in decision. <sup>2</sup>Both Sierra and Pamela made the decision that they wanted to stop taking their antidepressants for pregnancy, and started tapering down their doses preconception. They both conceived before they finished the tapering process and completely stopped the medication in their first trimesters.
### Pseudonym | Preconception | 1<sup>st</sup> Trimester | 2<sup>nd</sup> Trimester | 3<sup>rd</sup> Trimester | Decision status at time of interview
--- | --- | --- | --- | --- | ---
Najdah | Undecided; ↓ | - | - | - | Undecided
Pamela<sup>2</sup> | No; ↓ | No; | No | No | No
Sofia | Undecided | - | - | - | Undecided
Rachel | N/A (unplanned) | No; | No | No | No
Madison | Unclear<sup>3</sup> | No; | No | No | No
Olivia | Undecided; ↓ | - | - | - | Undecided
Tara | No | No | No | No | No
Wakana | No | No | No | No | No
Vanessa | N/A (unplanned) | No; | No | - | No

**Notes.** ↓ = attempted to decrease dose; ↓ = decreased dose; ↑ = increased dose; ⬤ = stopped medication; ➔ = switched medication; - = not applicable at time of interview; bold = change in decision. <sup>2</sup>Both Sierra and Pamela made the decision that they wanted to stop taking their antidepressants for pregnancy, and started tapering down their doses preconception. They both conceived before they finished the tapering process and completely stopped the medication in their first trimesters. <sup>3</sup>Not clear from the interview if decision was made preconception or only after pregnancy was confirmed (Madison was trying to conceive with fertility drugs, but still using antidepressants until pregnancy was confirmed, at which point, she stopped antidepressants right away).
### Table 2.2. Participant characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage in the perinatal period at time of interview</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preconception</td>
<td>8</td>
<td>25.8</td>
</tr>
<tr>
<td>Pregnant</td>
<td>23</td>
<td>74.2</td>
</tr>
<tr>
<td><strong>Number of living children (in addition to fetus, if pregnant)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>9</td>
<td>29.0</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>3.2</td>
</tr>
<tr>
<td><strong>Romantic partner</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>29</td>
<td>93.5</td>
</tr>
<tr>
<td>No</td>
<td>2</td>
<td>6.5</td>
</tr>
<tr>
<td>*<em>Lifetime psychiatric/neurological comorbidity (with depression)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>23</td>
<td>74.2</td>
</tr>
<tr>
<td>Eating disorder</td>
<td>7</td>
<td>22.6</td>
</tr>
<tr>
<td>Post-traumatic stress disorder</td>
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<td>12.9</td>
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<td>Substance use</td>
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<td>Brain injury</td>
<td>3</td>
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<tr>
<td>Obsessive-compulsive disorder</td>
<td>2</td>
<td>6.5</td>
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<tr>
<td>Bipolar II disorder</td>
<td>1</td>
<td>3.2</td>
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*Notes. *Self-reported by participants; many participants reported multiple diagnoses*
Data were not collected systematically regarding ethnicity, education, or occupation; however, some participants spontaneously disclosed this information. Reported ethnic/racial backgrounds were: white (n=11), Asian (n=8), and Latino (n=1) (11 unknown). Five participants reported being immigrants to Canada - from South Africa (n=2), Japan, India, and Mexico, and five reported being first generation Canadian (parents emigrated from South Asia (n=2), Eastern Europe, China, and Japan). Reported highest educational backgrounds were: high school (n=1), college/trade school (n=3), undergraduate degree (n=1), Master’s degree (n=4), PhD (n=3) (19 unknown). Almost 3/4 of participants (n=22; 71%) shared information about their occupational status. Eleven participants worked in healthcare or childcare (e.g., nurse, occupational therapist, genetic counsellor, dental assistant, nanny); five participants worked in the arts (make-up artist, music teacher, yoga teacher, animator, or interior designer); three participants worked in the technology industry (including as an engineer or on the business management side); and three participants were on leave or income assistance. Home address was available for almost all participants (n=27; 87.1%): 23 lived in an urban or suburban area; and four lived in rural areas.

**Decision making regarding antidepressants in pregnancy: A constructivist grounded theory**

This feminist grounded theory places the woman in the centre of the model and DM process (Figure 2.1). This woman has a history of depression, and is in the perinatal period (the purple circle in which the woman and DM process are embedded). The perinatal period is set within the large square box, which symbolizes the societal environment in which she is making decisions about antidepressant use in pregnancy. Aspects of the societal environment that are particularly influential on her DM are: 1) patriarchy, 2) stigma, and 3) privilege. She can enter or
re-enter (the purple arrows) the DM process (the blue circle) from any stage in the perinatal period. Her DM process is complex and dynamic; there are no discrete stages or phases. Three emotions – anxiety, guilt, and fear – dominate her DM processes. These emotions come and go, but are powerful factors that influence how she experiences making her decision(s). These acute emotions emerge from within the more general emotional/cognitive environment that is present during the DM process.

There are three clusters of activities (gray circles), which are strongly connected to one another. These clusters are: 1) Seeking information, 2) Making sense of information, and 3) Self-soothing. In ‘Seeking information’, she explores internal reflection, consultations, and written information, with a focus on risks – to herself and her baby – and strategies to minimize these risks. In ‘Making sense of information’, she appraises information for its trustworthiness; reflects on her beliefs; engages in thought experiments; explores ways to see the information from different angles; and integrates information to evaluate risks of harm. In ‘Self-soothing’, she manages the negative emotions of anxiety, fear, and guilt, by repeating a mantra; normalizing; gatekeeping; and building a safety net. She moves back and forth between these clusters many times, and in many ways, which is represented by the double gray arrows going in both directions between the smaller gray circles.

In order to reach a decision (the white circle), she engages in further DM processes for synthesizing information to get from the ‘Making sense of information’ cluster of activities or the ‘Self-soothing’ cluster to a decision (represented by the black arrows from those two clusters to the white ‘decision’ circle). These processes are: 1) evaluating information for its consistency between sources and congruence with their beliefs, and 2) assigning weight to information. If she reaches a decision, it isn’t necessarily final. The white decision circle has a dotted outline to
show that it is not a permanent state. She could return to the DM process and either confirm or change her decision later. This is depicted in the diagram with the small white arrow going from the white decision circle into the blue DM process circle.

Elements within the model are highly interconnected and overlapping. To avoid redundancy within this chapter, I have chosen to present concepts in one place in which they appear within the model, and then to reference their connection to other places, including the page number to facilitate review, if desired. I have also presented smaller versions of the model at key points within the chapter, highlighting areas of foci using red font to support the reader in digesting the theoretical model and reinforcing connections between textual and graphical representations.
Figure 2.1. Decision making about mental health care in relation to pregnancy: A constructivist, woman-centred, grounded theoretical model.

**: woman who has experienced depression

**Blue circle**: The decision-making process, within an emotional & cognitive environment

**White box with solid black outline**: Societal environment underlying, and influencing, the decision-making process

**Shapes with dotted outlines** (purple & white circles, & white boxes for emotions): Transitory states influencing movement within the decision-making process

**Solid gray circles**: clusters of decision-making activities

**Gray/black arrows**: Processes connecting clusters of activities to each other (gray) or to the outcome of decision making (black)

**Purple/white arrows**: Possible starting points from which participants entered the decision-making process (stage in perinatal period or from a decision)
Contextual factors: The decision-making environment

Contextual factors are many-layered and extremely complex. These factors are intimately connected and overlapping, and collectively comprise the environment in which individuals make decisions. A variety of these factors interact to create power differentials within the DM environment. Two aspects of the DM environment were most salient when women were deciding about antidepressant use during pregnancy: 1) emotional/cognitive; and 2) societal. These two aspects are represented in Figure 2.1 (page 59) by the blue circle, and the white box with a solid black outline, respectively.

The decision-making environment: Emotional/cognitive aspects

Participants’ emotional and cognitive environments (components highlighted in red in Figure 2.2) exerted an impact on their DM over three temporal frames: 1) long-term (years) - their past experiences with depression and other mental illness, 2) medium-term (months) – their experiences of mental health or illness around the time of DM, and 3) short-term (days) – specific emotional/cognitive experiences occurring acutely within the context of DM. The long-term emotional/cognitive environment was most relevant to the ‘seeking information’ cluster of DM activities (page 77). The medium-term emotional/cognitive environment was most relevant to the ‘making sense of information’ cluster of activities (page 89). The short-term emotional/cognitive environment was most relevant to the ‘self-soothing’ cluster of activities (page 109). Overall, participants observed that symptoms of depression and anxiety had a disempowering impact on their experience of DM, and conversely, participants felt empowered when they perceived that their treatment approach was keeping symptoms of mental illness well controlled.
Figure 2.2. Theoretical model of decision making (DM) about mental health care in relation to pregnancy, with red font highlighting the emotional/cognitive DM environment. The long-term emotional/cognitive environment is represented within the woman in the center. The medium-term emotional/cognitive environment is represented within the blue DM process circle. The short-term emotional/cognitive environment is represented by the boxes with broken outlines labelled “anxiety”, “guilt”, and “fear”.

Impact of depression/anxiety on the overall DM process/outcome

Participants identified some depression symptoms as having a negative impact on DM in general, such as apathy, withdrawal, lack of motivation, hopelessness, lack of energy, and poor cognitive functioning. A few participants also commented on experiencing a lack of insight and how their perinatal mental health treatment plan included other people in order to overcome this potential barrier to effective treatment DM.
Basically, [my husband] is really good at letting me know, in a very kind way, that I can receive... that maybe we should do something about this. And so, I feel he’s going to be a good gauge for me as well. Because sometimes when you’re in the zone, you don’t even realize, like you’re not very self-aware. That’s the problem. – Tara, third trimester, not taking antidepressants

Participants with anxiety disorders devoted a great deal of energy to DM in the preconception period. Some participants with anxiety commented on how their experience of anxiety negatively impacted their DM process overall.

I think I tend to be more concerned about the less likely problem than all the more likely benefits, in almost any situation. That’s probably part of my anxiety problem. I mean I can see the difference, I can see the pros and I can see the cons, I can logically see that. How I feel about it is not rational. – Stacy, third trimester, taking antidepressants

Impact of effective treatment for depression/anxiety on the overall DM process/outcome

A few participants who were taking antidepressants, and continued to take them during pregnancy, felt that their antidepressants had a positive impact on their mental health and cognitive functioning, and thus, also on their DM.

It was a pretty easy decision, and I think because [I was taking the antidepressants... if I hadn’t been] I wouldn’t have been in the head space to actually make the decision well. [...] if I was in my anxious crazy place that I was with the first pregnancy... it took me so long to go on medication... I was so resistant because I had really catastrophic and not realistic thoughts about it. Whereas, those thoughts were then under control... because I was already on the medication. So, it was a positive feedback loop. – Whitney, third trimester, taking antidepressants

The decision-making environment: Societal aspects

The societal environment is represented by the white box with a solid black outline in Figure 2.1 on page 59. Aspects of participants’ societal environment that were particularly relevant to their decisions about antidepressant use during pregnancy included: patriarchy (both
in healthcare specifically, and in society more broadly); stigma; and privilege. These aspects are highlighted in red in Figure 2.3.

**Figure 2.3.** Theoretical model of decision making (DM) about mental health care in relation to pregnancy, with red font highlighting the societal DM environment, and aspects of it that were particularly relevant to women’s decisions about antidepressant use during pregnancy.

Patriarchy manifested as relevant to the DM process in two main areas: 1) health care, and 2) with respect to societal expectations of women. In health care, health care providers controlled access to information and also to opportunities for care. Societal expectations of women during pregnancy emphasized a woman’s responsibility for ensuring a positive outcome in terms of her baby’s health, and expected women to prioritize their baby’s health over their own health. The
stigma of depression and the stigma of psychiatric medications, in conjunction with societal expectations of women in pregnancy, compounded in an even greater stigma of psychiatric medication use in pregnancy, which was highly influential in participants’ DM. Multiple sources of privilege impacted participants’ DM, including: 1) economic/class; 2) educational; and 3) geographic privilege. Each of these aspects of privilege acted as a barrier or facilitator to accessing care and supporting participants’ overall DM experience.

Patriarchy

Societally, I mean, I'm certainly not immune. We live in a patriarchy. We live in a mother shaming culture. – Rebecca, third trimester, taking antidepressants

Patriarchy in health care: Controlling the light over the black box & gatekeeping

The position of power held by health care providers – particularly physicians – in relation to patients, is rooted in patriarchal values. This power differential between providers and patients was highlighted in several ways in the interviews. Providers controlled access to information, with scenarios shared in which some participants did not receive information when they were seeking it, or were surprised by information when it was not requested. Providers also controlled access to care and opportunities for treatment. Some participants also faced resistance from providers regarding their treatment preference (page 123). Lastly, a few participants felt hesitant about expressing their point of view due to the power differential between themselves and their providers.

Provider control of the light over the black box: Access to information

Some participants reported that they did not receive information relevant to the decision about antidepressant use in pregnancy (e.g., either risks to themselves or risks to their baby of taking antidepressants or not taking antidepressants) when they were seeking it from physicians.
Instead, they often received the physician’s clinical opinion, without all the details supporting it. In some cases, physicians expressed the opinion that it was best not to take antidepressants during pregnancy, and in other cases, that it was best to take antidepressants. It seemed from the interviews that, when physicians emphasized the benefits of taking antidepressants during pregnancy, they may have neglected to fully share what is known about the risks of antidepressants during pregnancy. However, all participants in this situation expressed the desire to know about the risks of taking antidepressants. For example, Molly shared that her reproductive psychiatrist focused on the benefits to her and the baby of continuing her antidepressants, and emphasized that antidepressants are low risk. Molly related that she had not been informed about risk in a numeric way, although she would have been interested in hearing the information presented in that way.

Yeah no, if there were numbers I'd love to hear it, but so far, it's been really general that it's a low risk medication. – Molly, third trimester, taking antidepressants

Sofia had consulted with a family doctor and an obstetrician regarding antidepressant use in pregnancy and had only been given advice, without information.

Doctors are really … I feel like they don’t give a straight answer. I feel like, maybe, they’re risk managing, instead of actually giving you all the facts so you can make the … decision. Or telling you, a certain percent of chances, these are the chances of something happening, and if something happens, it could be this, or this, or this. And then you can at least … I don’t know… make your own decision […] ‘cause yeah… you only get the ‘yeah, you can do it’ or ‘no, you shouldn’t do it’. – Sofia, preconception, undecided

When these participants received more information later on from other health care providers, media sources, or friends/family, their trust in the original provider from whom they sought information was undermined, to some extent. A couple of participants, such as Audrey, who put a lot of weight on the trust they had in their health care providers and support team in
the initial decision to take antidepressants in pregnancy were later surprised by information –

received from a different health care provider – about the possible implications of that decision.

I didn’t [do any of my own research] when I decided to take the medication. I think it was because I was so overwhelmed and stressed that I just let her [my RMH psychiatrist]. [...] I’ve recently realized, and I’m still making the decision right now, because I wanted to come home after the baby [was born] fairly soon but, because I’m taking an SSRI, the baby is at risk for Neonatal Adaptation Syndrome, which no one had brought up to me before, which then you’re expected to stay in the hospital for screening longer, and I actually didn’t know that. So that was a little bit of a surprise and then I felt some guilt over that because it pretty much feels like you’re giving your baby a drug and they’re going to go through drug withdrawal because of what you’re doing. I felt a little bit frustrated that [my psychiatrist] hadn’t said anything because at first, I wondered if she knew, and then I realized because of where she works, she probably does. I also realized that maybe the risk was so small that it wasn’t a huge deal, but I would have liked the opportunity to discuss it with her since she was the one that provided the medication but, because of how fragmented the healthcare system is, that won’t happen until after the baby’s born in about a month. [...] I guess everyone talks about, and that’s been the recurring message about, how safe it is to take them, which I do agree, but it’s still nice to know the risks if you’re going to be given this piece of research at the end that says you need to stay in the hospital because of X, Y and Z. – Audrey, third trimester, taking antidepressants

Provider gatekeeping: Access to treatment options

Some participants’ treatment preferences conflicted with their providers’ recommendations (page 123). While some participants acted on their own preference without the support of their provider (for example, by discontinuing their antidepressants), a few participants (such as Pamela) felt that they needed their provider’s support before they changed their treatment plan. These women didn’t simply stop taking their medication unsupervised – rather, they persisted in asking their provider to support their decision.

I went to my doctor and said, “I want to start getting pregnant in the next year; this is my goal [to stop taking the antidepressant].” He said he didn’t think it was a good idea, and he would like me to remain on it. And so I went in there multiple times to finally convince him to write me a lower prescription (laughs). – Pamela, third trimester, not taking antidepressants
In other cases, participants were not able to adjust their treatment plan as they desired without the support of their provider. Jane, for example, had done a lot of research preconception, including consulting with a reproductive psychiatrist, and had concluded that continuing to take antidepressants during pregnancy was the right choice for her. In her first trimester of pregnancy, when she noticed an increase in her symptoms, she went to her family doctor to ask for a prescription for a higher dose. Her family doctor didn’t feel comfortable supporting her in that plan – pointing to the Health Canada warning attached to the medication (Paxil). Jane then had to challenge her family doctor in order to convince her to support her choice, which felt uncomfortable.

When I went to see [my GP] during the early pregnancy, I wanted to increase to 15[mg], because my anxiety was coming back really badly. And she was like, “I don’t want to do this. I don’t want to increase...” And I’m like, “No, I know, I’ve done the research. The psychiatrist said it was fine”. So, I had to actually push my GP, which created anxiety in me, because she just pulled out the thing, and it’s like: Do not take while pregnant. – Jane, second trimester, taking antidepressants

Other participants were not able to resolve the conflict between their preference and their providers’ preference(s) and delayed their decision. Sofia was in this position, and felt unsupported by any of her providers to wean off her antidepressants in advance of trying to conceive.

I did tell the psychiatrist when I was seeing him, “What if, in the future, I wanna try to get off it, and see if I’m okay without the medication?”. And he said that it’s really dangerous and it makes him really nervous... that I would have to either be an inpatient or have a mental health thing that I’m checking with every other day or every day. Because it makes him really worried that I will be in an unsafe place... because of what happened last time, which may mean that I may try to commit suicide. One of the things why I asked him about this was because at that point, I was 26, and was like, maybe at one point when I wanna have a child, and I might not wanna be on the medication... could that ever happen? Could we try it before I get there to see if it’s a possibility? I talked to my GP and I said, “What if I don’t want to be on this? Or what if I wonder if I can ever do without it?” And he tells me, “No, no, too dangerous, no. The psychiatrist put you on it, I’m not going to take you off it.” I felt like shut doors. – Sofia, preconception, undecided
A few participants, like Stephanie, were acutely aware of the power differential between themselves and their provider, and were hesitant about asserting their point of view.

Catriona: ... [your doctor] was saying if it gets really severe then she's going to want to, I think you said “put her foot down” in terms of the antidepressants. So, how does that make you feel?

Stephanie: Terrified. [...] I know that doctors are allowed to fire patients and I don’t want it to get to that ‘cause she's a really good doctor. But at the same time, I think I've not gone in-depth enough with her in terms of what my experience has really been like. And I'm starting to think that maybe that would be a good idea. – Stephanie, third trimester, not taking antidepressants

A few participants saw the need for referrals and having to enter the healthcare system as a barrier to accessing support for their mental health.

Not all women go to doctors, not all women want a referral, not all women know... I mean, I didn’t even know that the Reproductive Mental Health clinic existed until my doctor referred me, and then there’s some amazing things that they have, some really great little programs and stuff like that. But again, it’s so limited... it’s only the women that get referred to... and understandably... not at all a knock against them, but it would be really nice to see community centres offer something like that. I think just having it more in the public sphere... that sort of support group, but without having to have gone through the system to get to that help. I’ve always found that that’s been a barrier for me - the cost of mental health programs, the referral program that has to be in place. – Samantha, preconception, planning to take antidepressants

**Societal expectations of women**

It was clear from the interviews that women in this study had internalized the message that society expected them to assume the majority of the responsibility for childbearing and childrearing, including any related DM.

I still feel guilty when my husband has to do stuff sometimes, but I try not to feel as guilty as I did before. – Natsumi, second trimester, not taking antidepressants

Most participants commented on how ‘weighty’ the decision felt regarding how to manage their mental health during pregnancy. They felt an acute sense of responsibility as a mother or prospective mother.
I mean, the main thing is that you’re considering another human life, right? It’s not just you, it’s another human. So, yeah, I would say the decision seemed a lot more weighty. – *Jane, second trimester, taking antidepressants*

I ask all the questions, I try to see everything. Especially because you’re making the decision, not for your own life, but for somebody else’s life. And it is really scary, ‘cause when you’ve been in that hole, you know what it is. And like, at least for me, bringing another human being, that’s a big responsibility, and you don’t want to drag them with you through that hole. I don’t want to be so depressed that I cannot take care of the kid. - *Sofia, preconception, undecided*

In addition, participants commented on the prevalence of societal messaging requiring restrictions during pregnancy, for example, regarding diet. These pressures led many participants to experience a state of hypervigilance and anticipatory guilt in the event of something being “wrong” with the baby.

If she comes out with something, there’s definitely going to be some blame there. I’m going to think it’s my fault. What did I do, what did I eat, what did I . . . what did I do wrong? And they put so much emphasis now on pregnancy on so many things, like “Don't have a sip of wine. Don't eat sandwich meat. Don't . . .”, just absolutely every single thing. – *Stacy, third trimester, taking antidepressants*

Connected to this, many participants spoke about societal expectations not to take medications during pregnancy; with some commenting specifically on a moral judgment that avoiding medication in pregnancy is the “right” choice.

I think part of it is that you want to go off [anti-depressants] for other people, right? You want to go off because that’s the right thing to do, not because it’s the best thing for me to do. Because it’s really hard to admit and say, “I feel good on these, so I’m going to be selfish and stay on that”. I also don’t want to be stigmatized, like, “Oh, she’s on medications when she’s pregnant”, it’s terrible. So, I think a lot of it is the pressure of the society, of having this perfect, clean, natural, don’t-do-any-of-those-things, you know what I mean?” – *Samantha, preconception, planning to take antidepressants*

Some participants, including Samantha and Carolyn, commented on societal pressure to have a “natural” pregnancy, which required avoidance of all medication during pregnancy.

There was a little bit of the pressure of the medication and baby at the same time ... you want to have that pure, and not have to take anything... just take a prenatal vitamin, don't worry about analgesics during delivery, you don't need them, have it in your bathtub... it's
going to fine. There was a little bit of that, but at the same time, I've never been that kind of person, like I went into pregnancy thinking - when it comes to the end, bring on the drugs, sign me up! – Carolyn, third trimester, taking antidepressants

Some participants also mentioned instances when physicians reinforced this belief that women should avoid medications during pregnancy.

... part of my back pain is related to nerve pain. I had spoken to somebody, and they had said, “Well, we can't give you medication because you're thinking about getting pregnant.” So why would you be able to take other medications? – Lena, preconception, undecided

Some participants observed ways in which society, and the healthcare system, focused almost completely on the baby and its health, at the expense of any substantive consideration of the mother’s health.

Prenatal classes talk about childbirth and then after, how to breastfeed your baby and stuff. But there’s no aspect of like what can happen to the mom, and how you deal with sleepless nights, and how do you deal with the pain of C-sections or labour and birthing? It’s so lightly touched upon that you assume, “Oh, either that’s not important, or that doesn’t happen, or it’s uncommon.” And I don’t understand why the health of the mom or the parent isn’t as highly emphasized. It’s all about the baby, which I mean, yeah, the baby is important. But if you’re not there to take care of the baby, then what’s the point? - Natsumi, second trimester, not taking antidepressants

A few participants identified explicitly that they felt pressure from society to sacrifice their own needs for their baby.

For the most part, I didn’t really talk about it [taking an antidepressant during pregnancy] with anybody, because I was afraid that people would judge me, because there’s a lot of pressure to do what’s best for the baby and sacrifice, and I really wanted to do that, but it just didn’t work out [tearful]. – Nadia, third trimester, taking antidepressants

Taken altogether, these expectations for female gender roles resulted in a default position for most participants whereby they de-prioritized themselves relative to others, especially relative to their developing or potential (in the case of women who were preconception) baby.

It was hard to remember that my mental health was a benefit. That's a really hard one to pull out from everything else and say, "Oh yeah, there's risk/benefits. The risk to the foetus, but the benefits is decreased in delivery and-" , but you forget that the biggest
benefit of all is your own mental health and your ability to make rational decisions, your ability to carry through a health pregnancy... continuing to exercise, continuing to eat well, sleep well... Like, you also have benefits... you are not just a shell... a vessel.” – Carolyn, third trimester, taking antidepressants

Stigma

All women commented on the stigma of depression, with most attributing it to a lack of societal understanding of the experience and causes of depression.

There’s so much judgement about it because of, in my opinion, a lack of understanding of what it actually means. It’s not like a lack of seeing one’s worst or, being ungrateful or being lazy, or whatever other – I mean, there are so many different ideas of what people in depression really is. It’s none of that. But I definitely feel like ‘put on your big boy pants and just deal with it’, you know? Like, what’s your problem? And that’s what’s expected, and it’s so much more complicated than that, and I wish to whatever, whoever, however, that it were simpler. And it’s just not. So, there is a sense of guilt that I have, because of that projection. – Hazel, third trimester, taking antidepressants

Many participants discussed how the stigma of depression caused resistance to talking about the experience of depression, and to seeking help for symptoms.

There are so many undiagnosed people out there that do need help or that could utilize something like that instead of the alternatives that they’re doing. It’s definitely a very touchy subject with some people and not everybody’s as open. I still am scared to talk to people, but if someone has been like “I’m going through a hard time, I’m really depressed.”, then yeah, I’m willing to be open. – Pamela, third trimester, not taking antidepressants

In addition to the stigma of depression, most participants who had taken antidepressants discussed the stigma of psychiatric medication use.

It does take quite a lot of convincing for me to take medications. When I was first offered the medication, I felt those feelings of failure again. I’ve kind of worked through the stigma of having to take psychiatric medication; that’s been part of what I’ve worked through personally over the years. – Olivia, preconception, undecided

Some participants connected this with the absence of a belief at a societal level regarding the necessity of antidepressants.
I know there are people out there who do have extreme views about antidepressants, and just in use generally and not specifically even in pregnancy, but that, you know, they’re a crutch and all that kind of stuff. – Nadia, third trimester, taking antidepressants

Some women also shared how their own stigma related to taking antidepressants lessened after they found antidepressants that were effective.

If I talk to another friend or a mom that I’ve had post-partum, I usually do say that I've taken antidepressants and that they've been helpful... I don’t have a negative perception of them anymore because I think they're really helpful. Sierra, second trimester, not taking antidepressants

The stigma of depression, and of taking antidepressants, in combination with societal expectations of women (page 68), culminated in compounded stigma of taking antidepressants during pregnancy.

It’s about this media, it’s about people saying why would you ever... from somebody who doesn’t have anything, who doesn’t smoke, drink or take any kind of drugs that they need, they wouldn’t understand... why in the world wouldn’t you stop taking this drug [during pregnancy]? But it’s not about toughing it out, it’s not about not being able to take Ibuprofen because you have a headache, because this is a serious... it’s so much more impactful than they think it’s going to be. Our society think it’s an elective thing, when it’s really not an elective thing for a lot of people. And I think that’s the thing, it’s important that they know this is not an option. – Samantha, preconception, planning to take antidepressants

A consequence of this compounded stigma that many participants discussed was a lack of openness about the experience of taking antidepressants during pregnancy. Most participants who took antidepressants prenatally reported mainly keeping the decision to themselves (page 114). Consistent with that, most participants (regardless of their own choice) were unaware of anyone else who had made the decision.

I’ve never met anybody that has openly acknowledged that they have depression [in pregnancy] … I have a friend who I suspect might have depression, but she never says it out loud so I cannot… ‘cause I feel like a lot of it, at least my friends, they have this expectation, ‘Oh I’m pregnant, I should be happy, happy, glowy, glowy, right?’ So far nobody has ever admitted otherwise. Or has not openly told me, ‘I’m taking antidepressants.’ Because I feel like it’s something that a lot of people would not share so openly... everybody keeps it so hush hush. Nobody wants to say it, ‘cause they don’t
know how people are going to take it. So, it’s like… you can’t really find it out there. – Sofia, preconception, undecided

Privilege

All participants commented on ways in which they had experienced advantages or disadvantages in terms of accessing care. The majority of participants identified that, unfortunately, access to mental health care is not equal across the population.

I’ve been lucky - we both have had extended insurance. And I remember when I was on my medical break once, we paid through our pocket. But I’m also coming from a privileged step; not a lot of people have that. And sometimes four hundred dollars isn’t enough to see a counselor, you need to see the counselor a lot more times. – Najdah, preconception, undecided

Economic & class privilege

The cost of counselling was mentioned by most participants as a barrier to accessing optimal mental health care.

It all involves money and everything’s like two hundred dollars an hour and it’s just like, “okay, well, I don’t really have five grand to spend on ten sessions (laughs)”. And then, even if I managed to get myself into like two or three sessions, the lineup is six months to a year at some of these places. And just to get assessed is two hundred dollars. And most health care plans don’t cover it, so it’s out of your pocket, and right now is probably not the right... even though I would love to even try one just for the sake of it, for benefit and for education and just to have it on hand... it’s not really feasible, you know? [...] it’s like “Hi! I’m on EI, I’m not working, and I live in Vancouver of all places, which is the most expensive place to live (laughs)”. It’s sad... you have to be super upper class, you can’t even be middle class and afford it.” – Pamela, third trimester, not taking antidepressants

Costs of other mental health management strategies were also discussed, for example, yoga and exercise classes. If participants sought counselling through the public system, they had less flexibility in terms of choosing someone with whom they felt a good connection. Furthermore, the majority of participants raised that long wait times in the public healthcare system had detrimental consequences on their DM.

I see a lady for counselling at the same place, every two weeks. I wish it was better. It’s a lady that I used to see when I was about thirteen or fourteen years old. She was one of the
first counsellors I had tried. It didn’t work out for me, so I stopped seeing her. And then they were offering some free counselling at the place that I was going to for the group one, or whatever, some individual counselling [during this pregnancy]. And they just kind of put me with her. So, I’m seeing how it goes to see if there’s something new that she’s learned over the years. Or maybe I’m more level-headed and I’m more open to her suggestions than I was when I was a lot younger, but … Sometimes I go there it helps, and other times it just feels like it was a waste of time. You get given who you get given. I’m sure if I said something to them, they might put me with somebody else, but I might have to go back on the waitlist again. – Madison, third trimester, not taking antidepressants

A few participants, such as Sherry, commented on how symptoms of mental illness can interact with the limitations of the public healthcare system to amplify inequities in perinatal mental health care.

I made my appointment in the middle of my pregnancy at 20 weeks when I was really freaked out. I got it a week after he was born. It was my first appointment. That’s not acceptable. I luckily have a lot of skills and stuff like that, but what if my anxiety kicked in, or all of a sudden I got a bout of depression? […] I only have a window that I’m going to get help, and then I’m just going to sit at home and cry. People get worse and worse and worse where they just spiral and they’re not going to leave their house. The therapist is always like, “Well, you missed our appointment.” “Well, I have a disease where I miss things, genius. It’s almost like I have anxiety. It’s almost like I’m sad. Isn’t that one of the symptoms? Not doing things. You dick.” “Well, just get out of your house more.” “Go fuck yourself. How about that?” – Sherry, preconception, planning to take antidepressants

Participants with economic/class privilege were able to circumvent the challenges of long wait times, constrained appointment times, infrequent appointments, and lack of choice in provider by accessing perinatal mental health care privately.

I found a new doctor. I’m actually going to a private health care clinic in Vancouver that, you know, basically they go above and beyond to get you the help that you need… my dad was going to that clinic himself, and he suggested that I go, and he’s been paying for me to go. It’s just a totally different system where, you know, all the appointments are half an hour long and they take as much time as they need. I wish everybody could have a doctor like that. Anyways, I’m lucky that, for now, I get to see them. […] I have been seeing a psychologist that works at the clinic and I see her about every other week for CBT and exposure therapy for the anxiety. I was also diagnosed with OCD so that’s something that we’re working on also. - Nadia, third trimester, taking antidepressants
Educational privilege

Three types of education/training supported participants’ perinatal depression treatment DM, namely: 1) research, 2) healthcare, and 3) childcare. Many participants with a background in research or healthcare, such as Jane, identified that they had an advantage in being able to access information they considered to be trustworthy and relevant to the decision, and critically evaluate this information (page 91).

I think any woman considering getting pregnant that has access to some kind of a medical background, or a research background, is in a real position of advantage for decision making, because, yeah, I feel really bad for the women who are just going off what they’re getting from the news, you know? [...] I feel like, because I’ve had access to this information and the support, I’ve had to wrestle with that decision a lot less. I think, having had the support and the access I did, to make this decision, has probably helped my mental health a ton. – Jane, second trimester, taking antidepressants

A background in healthcare also facilitated participants’ access to care and providers who could support them in making sense of information and reaching a decision. These participants, such as Audrey, had a strong knowledge of how the healthcare system works and were better positioned to advocate for themselves, request referrals, and access care sooner.

I found a doctor here, and I actually asked him for a referral to the RMH program explicitly for more preventative reasons because I was starting to have some anxiety about getting depressed. – Audrey, third trimester, taking antidepressants

Conversely, some participants without ‘insider’ knowledge of the healthcare system expressed frustration about the lack of public awareness of the Reproductive Mental Health program, and that family physicians or maternity care providers hadn’t offered them referrals to the program.

I didn’t even know there was a Reproductive Mental Health clinic, and I know everything about this stuff. If [partner]’s co-worker hadn’t said, “Dez needs to go to this clinic,” I wouldn’t have gone to the clinic. My doctor doesn’t tell me anything. One of our good friends, his sister just got pregnant and she’s got a lot of stuff going on... I think there’s like bipolar... she just stopped all her meds. Just got pregnant, is doing so horrible, and she’s like, “What do I do? Can you ask Dez where do we go?” Ask Dez? Like why the fuck aren’t your doctors being like -? Because the doctors are just like, “No, stay on your meds.” Well, that’s not good enough. People need more. So, I sent her the number and I
said, “Just call them and they’ll at least like get your-” but then you’re doing all the work. – Desiree, preconception, undecided

A few participants commented on how their background in either healthcare (such as Twyla) or childcare (such as Sherry) shaped their beliefs regarding the relative risks of harm to mother and baby in the context of treatment for perinatal mental illness, which gave them more confidence in navigating this decision. Their education/training experiences informed their belief that a mother’s health is important, and a risk to a mother’s health also entails a risk to a baby’s health.

Being a [health care provider], there’s no doubt that that comes into it for me. Just the paradigm that there are some medications that are needed, you know? And even if there are some risks, sometimes those risks are worth taking. – Twyla, first trimester, taking antidepressants

I’ve nannied since I was 19, and so I’ve been around a lot of moms and stuff like that. It’s just like, you have to take care of yourself first. That’s number one. You have to. Just put the baby down. Put him in a rocker. Walk away and do what you need to do... mental health is so important on that. When it’s somebody else, it really put it in perspective for me. – Sherry, preconception, planning to take antidepressants

**Geographic privilege**

A minority of participants (n=4) lived beyond the suburbs of a major urban centre, and identified that there were limited mental health care options in their geographic region.

Any health groups or anything like that that are in the area that I live in ... I try to look those up. But there is not a whole lot here. If I lived an hour out of town, there’s lots of help. But where I live, there is not a whole lot. – Madison, third trimester, not taking antidepressants
Cluster 1: Seeking information

Seeking information is one of the three clusters of DM activities (represented by the smaller gray circles in Figure 2.1 on page 59) within the DM process (represented by the blue circle in Figure 2.1 on page 59). This cluster is highlighted in red in Figure 2.4.

Figure 2.4. Theoretical model of decision making (DM) about mental health care in relation to pregnancy, with red font highlighting the ‘Seeking information’ cluster of DM activities, within the DM process.

All participants sought information to inform their decision about using antidepressants during their pregnancy, but variation was observed in the topics and sources of information sought, and the extent of information-seeking behaviour. Broadly, information seeking was focused on two main topics that were considered by all participants: 1) risk of harm to self and
strategies to mitigate this risk, and 2) risk of harm to baby and strategies to mitigate this risk. Sources of information included: internal reflections (e.g., past experience); consultations with family, friends, or health care providers; and written information (including medical websites, blogs, online forums, textbooks, and peer-reviewed literature). Information seeking ranged from being relatively brief and superficial to extensive and thorough.

**Risk of harm to self**

Participants were acutely aware of the nature of the potential harm to themselves – they knew what it meant to experience depression as a result of their past experiences, and typically perceived their risk of experiencing depression during the perinatal period as high. Thus, they mostly focused on seeking information about treatment strategies to reduce their risk of a depression relapse in the perinatal period. Women sought information about the following risk mitigation strategies (to a greater or lesser extent): antidepressants; talk therapies (e.g., supportive psychotherapy³, psychodynamic therapy, cognitive behavioural therapy (CBT), dialectical behaviour therapy (DBT)); self-management options; self-care options; and the level of social support which they could expect during the perinatal period.

In terms of information sources utilized for this topic, they most often sought information internally – reflecting on their past and current experiences with depression and its treatment. Sometimes, however, women sought information – particularly about their current symptoms and the level and types of support that they could access – from others, including their partners, family members, and/or health care providers. It was relatively rare for women to seek written information on this topic, although it did occur when women sought information about treatment options they hadn’t already tried.

³ Formerly known as Rogerian psychotherapy
Participant’s past experiences with depression and other mental illnesses were diverse, but universally, women feared returning to that experience of despair. In particular, women who had been hospitalized for mental illness and those who had attempted suicide were concerned about that happening again.

I don't want to go back to the point where I started off, which was being suicidal and being in a psychiatric ward. [...] obviously I don't want to cause risk to the baby and … I don't want to go and wean down all these medications, or even stop these mediations, and then get pregnant, and then get to a point that I'm so suicidal that I cause harm to myself and to the baby. [...] my biggest concern is going back to a place that I've already been. I don't want to be trying to conceive, and then get pregnant, and then be at this really low point. I obviously don't want to then have to go and get an abortion or something. – Farha, preconception, undecided

Risk mitigation strategy: Antidepressants

Almost all participants (n=29, 94%) had tried antidepressants at some point in their lives. Thus, information seeking in relation to risk of harm to self as a result of antidepressants was mostly internal, although they did occasionally consult with health care providers, partners, or family members. Information seeking about antidepressants with respect to their risk for perinatal depression included: reflecting on their past experiences with antidepressants; reflecting on their current symptoms and level of mental wellness in relation to antidepressant use; and conducting physical experiments and monitoring impact on current symptoms. Given the close connection of these information-seeking practices to medication beliefs, illness beliefs, and an evaluation of the risk of harm to self, these are discussed in the next cluster of activities: making sense of information (page 89).

Risk mitigation strategy: Alternatives to antidepressants

Many participants also sought information about alternatives to antidepressants for managing their risk for depression, including talk therapies, self-management options (e.g.,
workbooks for self-administered CBT or DBT, bibliotherapy, or journaling), self-care (e.g., nutrition, exercise, sleep, taking time for themselves (NEST)), and social support. Women reflected on past experiences with talk therapies and self-management options, if applicable, to estimate the likelihood that engaging in such treatments again would lower their risk for depression. They also assessed their current level of mental wellness, in the context of strategies that they were employing, to inform their risk assessment for experiencing perinatal depression if they were able to continue engaging with these strategies. For some women, such as Vanessa, this information informed their decision to try pregnancy without antidepressants.

I just decided that since I was feeling good, and I’m doing everything else that I normally don’t do when I’m depressed, like staying close with family, exercising, eating right, seeing a psychiatrist… which are all things that help with depression... so I’m trying to treat it without medication right now. – Vanessa, second trimester, not taking antidepressants

For other women, like Stacy, it strengthened their conviction of the necessity of taking antidepressants during pregnancy.

I tried to talk to a counsellor. That was really frustrating because I was looking for her to give me a way to fix it, but she was just someone who listened. And I guess I didn’t need someone who listened. I needed to fix it. Do you know what I mean? Maybe some people just need someone to listen and they feel better. That wasn’t working for me. [...] And I tried St. John’s wort, and some other things that were just trying to help bring my heart rate down, or help me sleep better at night, or was I missing a supplement . . . went to a naturopath, helped nothing. [...] So I was trying to meditate, and tried workbooks about being in the moment and things like that, which is like, all good things, but not things that really helped me. [...] I’ve been on [Lexapro] since 2007. The same amount. I haven't needed anything else. [...] I didn't want to change the medication [for pregnancy]. That really freaked me out. It’s twice I’d been through that, and it was bad. It was so bad. So I anticipated the exact same thing. – Stacy, third trimester, taking antidepressants

Additionally, women gathered information about opportunities – and the feasibility of these opportunities - to expand their repertoire of mental health management strategies. These included: engaging with a new provider, pursuing a new form of talk therapy, prioritizing self-care or diversifying the ways in which they engaged in self-care, and strengthening their social
support. This information seeking was mostly internal, but also included some consultation with health care providers (particularly to explore new options for talk therapies), partners and family (particularly for exploring options to strengthen social support and self-care), and for a few individuals, searching Google for new therapy options and the feasibility of accessing them. The only information that participants sought online that was relevant to their evaluations of risk of harm to themselves was about depression treatment options that they hadn’t already tried. This was mostly limited to seeing what options existed, how much they cost, and whether they were geographically (or otherwise) accessible.

I went to another counsellor last year to try to prepare me for my next pregnancy. I see the necessity of it. It’s just the barrier of access or expense. It would be nice to have a counsellor who I clicked with, but I can’t find the right one. I’ll use them, perhaps, for a short time for a short problem, but I can’t find one that’s long-term. It would be really nice to have someone who just kind of... continued narrative instead of reintroducing every time... you've kind of laid down a foundation. [...] Even though my husband works for a multimillion dollar company, they don’t have any health benefits. It’s extremely frustrating. If financially it was easier to find a counsellor in the city, I think that would be a big help, to just have somebody consistent, like from before pregnancy to after pregnancy... having that same person there. – Natsumi, second trimester, not taking antidepressants

Risk of harm to baby

In order to assess the risk of harm to a baby from antidepressant use or untreated depression during pregnancy, participants tried to understand what might happen and how likely that outcome would be. Information seeking regarding the likelihood of the potential harm(s) to a baby was tightly intertwined with information seeking about the nature of those potential harm(s) and occurred concurrently. For most women, this was focused on the potential harm of antidepressants to a baby, but some women broadened their search to include the potential harm of untreated mental illness to a baby. In terms of information sources, they most often sought information externally – written information and consultations with health care providers,
friends, family, and partners. It was rare for participants to seek information internally on this topic, but it did occur for one woman (Sherry) who had taken an antidepressant during a previous pregnancy, and so was able to reflect on that experience when deciding whether to take an antidepressant in her next pregnancy.

**Seeking information: Broad**

Participants’ information seeking on this topic was typically broad – they didn’t usually have a specific potential harm that they were investigating. When seeking written information, most women conducted a broad Google search and paid attention to any information that appeared relevant.

I did do a lot of research, but I didn’t necessarily like what I read. And I know the internet is like the last place on earth you want to go to read anything... and forums and all that, because you know, it’s not a true study, it’s not a true form of this, but just hearing things that have happened kind of set the mood and mode for me to be like, this probably isn’t a good idea, because you could be the fifty out of a thousand or whatever. – *Pamela, third trimester, chose no antidepressants*

Many commented, however, that they had difficulty in accessing relevant and trustworthy information (page 91). One participant (Linda) shared that she hadn’t looked online because she didn’t know where to even begin to access relevant information.

Similarly, most participants came to appointments with health care providers with a vague desire to understand ‘the risks’, or to hear what the provider had to say about their situation generally. Participants most often wanted to understand the risks of harm to a baby from taking antidepressants during pregnancy, but some wanted to know about risks of harm to a baby from untreated depression in pregnancy.

[I just wanted to know] broadly if it would affect the development of the baby because typically any medication that you take, or anything chemical, or anything at this point, just in general in pregnancy, they say to be really careful of. – *Audrey, third trimester, taking antidepressants*
Many participants also asked their health care providers if they had cared for other patients who had taken antidepressants during pregnancy, and if so, what their experiences were with that.

[My reproductive psychiatrist’s] experience, her telling me that other patients have done it, her telling me that they’ve done it on very high doses and their children are fine. [...] That itself was huge for me. I need to know that I’m not the only one that was in this position. [...] I’m the kind of person that’s like - it’s not going to happen to me, deep down, so I feel like, if other people can, then I’ll be okay. So it kind of gives me that security. – Desiree, preconception, undecided

Some participants sought general information regarding risks for harm to baby due to taking antidepressants in pregnancy from friends and family members. This information seeking fell into two categories: 1) asking about someone’s personal experience with either taking antidepressants during pregnancy or stopping antidepressants for pregnancy; or 2) asking for their professional expertise – when they held a dual role of friend/family member and health care provider/researcher. Quite a few participants did have a friend or a family member who either had a personal experience of taking an antidepressant in pregnancy or stopping an antidepressant for pregnancy, or a vicarious experience – having heard of someone else with one of these experiences. Without exception, participants wanted to hear these stories. In the majority of these cases, the babies/children of women who had taken antidepressants during pregnancy were reported or observed to be ‘fine’.

I know people that have taken antidepressants through their whole pregnancy, and their babies are beautiful and fine. – Sierra, second trimester, not taking antidepressants

In terms of the other category for general information seeking from friends/family, quite a few participants had a friend/family member with professional expertise as either a health care provider or researcher, whom they asked about risks of harm to a baby due to taking antidepressants in pregnancy.

My friend is a physician who specialises in reproductive health. So she was a pretty good person to chat with about this. [Laughs] Being able to talk frankly with her was really
helpful... knowing at least one other person [a patient of hers] who has [had] a child after being on antidepressants... not the same antidepressants as myself, but seeing what happened after that pregnancy, and knowing, okay, well that was a scary situation, but they got through it, and what the child had [neonatal abstinence syndrome] was similar to what is the highest risk for... what I would go through. [...] it's like, okay, that is a possibility, it's going to be rough, but it can be done, and it doesn't have long-term effects. – Carolyn, third trimester, taking antidepressants

Seeking information: Specific

There were some scenarios in which women’s information seeking was more targeted: 1) when women had a high degree of medical literacy – from their education/training as a health care professional or from extensive experience acting as their own health care advocate; and 2) after a great deal of media attention on a research finding that suggested a particular harm to babies (e.g., autism) as a result of their mothers taking antidepressants during pregnancy.

Participants who were employed in healthcare often had narrower search strategies for information seeking. For example, Twyla – an allied health professional - focused her information search to specific websites that she perceived to be reputable, such as the point-of-care medical resource UpToDate and the Office of Teratology Information Services (OTIS, now known as MotherToBaby).

I also did a little bit of my own research by looking in like UpToDate and OTIS or whatever. – Twyla, first trimester, taking antidepressants

Participants, such as Farha, who had extensive experience acting as their own health care advocate often had more specific questions over the course of information seeking. Farha was taking multiple antidepressants, and wanted to know about the potential impact of taking those medications together during pregnancy.

[My reproductive psychiatrist] went through, like, this medication will do this harm to baby, this will do this, and then I asked, “okay, what is the research on, like, if you mix this medication with this medication? What will they do altogether? – Farha, preconception, undecided
Participants also had specific questions for their health care provider regarding a particular harm to a baby as a result of antidepressant use during pregnancy when research findings on the subject were in the news. In particular, during the first round of interviews for this study, there was a great deal of media attention on a study (Berard, 2016) that suggested there was an increased risk of autism for children of mothers who had taken antidepressants during pregnancy. Women in my study, such as Samantha, who were either considering taking antidepressants or who were taking antidepressants during pregnancy at that time, found these media articles alarming and discussed them with their health care provider(s).

I came in [to see my reproductive psychiatrist], like, the first week of January. I was like, “so this big site just dropped and you know...?” And it was interesting, because they sat me through, and they’re like, “Yeah, we’ve totally looked at this too, but you know here’s what” whatever it was, “like 87% chance increase”, you know, what it really means in [absolute] numbers, and they’re like, “yeah, okay, but those aren’t things they say in those [media] pieces, or like they don’t make it very clear, you know?” [...] and the other thing is that nobody’s writing articles that say: “Woman, you know, was off antidepressants and had this, this and this, and her child is this, this and this”, like nobody writes those. And really we don’t know if it’s these drugs that are doing it anyways. – Samantha, preconception, planning to take antidepressants

**Seeking information: How much?**

Participants’ information seeking ranged from being perfunctory to exhaustive. The extent of information seeking did not vary in any systematic way between seeking information about risks to themselves versus risks to their baby. Minimal information seeking occurred for women whose pregnancy was unplanned, who had decided about depression treatment in a previous pregnancy, or who were experiencing decision fatigue. In contrast, participants engaged in extensive information seeking when they: experienced anxiety; judged the information they had to be insufficient; or encountered conflicting information/beliefs/preferences.
Minimal information seeking

Only three women in this study had unplanned pregnancies (Linda, Rachel, and Vanessa), but their experiences were quite similar. They all stopped taking their antidepressants when they found out they were pregnant, after very short periods of information seeking. Both Linda and Rachel had decided not to take antidepressants in a previous pregnancy as well. When Linda found out she was pregnant, she did a little reading online about risks to a baby of taking antidepressants during pregnancy and stopped taking her antidepressant without consulting anyone.

With this pregnancy it was a little bit more rough, but I decided to do the same, I took myself off the medication. It was an independent decision. [...] I read a little bit online. I don't remember which website. [...] I did notify my family doctor once I found out I was pregnant that I did stop all the medication. [...] With my last pregnancy I wasn't on any medication either. I felt like I did okay. – Linda, third trimester, not taking antidepressants

Only one participant, Sherry, had taken antidepressants in a previous pregnancy, and she anticipated continuing to take antidepressants for her next pregnancy, without needing to do much information seeking.

We’re not even going to talk about it. I’m just going to be like, “Okay.” He came out in one piece. Everything was good. So far he’s great. I’m totally just going to do it. – Sherry, preconception, planning to take antidepressants

Participants also spent minimal time seeking information when they experienced decision fatigue. It was clear from the interviews that pregnancy required continual DM. For women nearing the end of their pregnancy, such as Audrey, energy available to devote to information seeking and DM was typically quite depleted. Audrey started taking antidepressants in the third trimester, and was subsequently told by her midwife that clinical guidelines recommend staying longer in the hospital after delivering the baby to monitor for neonatal adaptation syndrome if mothers had taken antidepressants during the third trimester. Audrey asked for written
information from her midwife to inform her decisions about continuing to take the antidepressants and how long to stay in the hospital following delivery.

I read through the information once, and I just decided I had made a decision, which doesn’t usually happen, but I think I’m just so tired of making decisions... I just made one... and yeah, I left a message for the psychiatrist and I don’t think she’s around, and so I figured I’d just take [the antidepressant] and see how the baby’s vitals are, and see how the birth goes. – Audrey, third trimester, taking antidepressants

Extensive information seeking

The most common association with extensive information seeking in the interviews was high anxiety. For the majority of participants, information seeking regarding risk of harm to a baby started with general Google searches. Most participants found the information that they accessed online to be alarming or overwhelming, and switched strategy to consult with a health care provider for information and/or advice rather than “Dr. Google”. Unfortunately, many participants spent quite a bit of time searching online and feeling anxious, before deciding to step away from the computer.

I kind of started with Googling, and looking up, and I’m like okay, I need to just – like there’s so much information out there... when it’s like just unfiltered Google information – not helpful. Takes you down a rabbit hole... I need to actually go see a psychiatrist, and see what they say. – Jane, second trimester, taking antidepressants

While anxiety often motivated women to switch from searching online to consulting with their health care provider, the reverse also occurred. It was much more rare for participants to return to searching online to validate what they had heard from a health care provider, but it did happen for some women with anxiety who were also highly medically literate.

Catriona: when you went home and had that chance to mull it over, did you do additional reading? Carolyn: Yah a little bit at that point just to say, "Okay let's just - I know she's right; I just need to read it for myself". – Carolyn, third trimester, taking antidepressants
Some women experienced an escalating cycle of anxiety-driven information seeking, which in turn fueled further anxiety, and more information seeking. In some cases, information seeking became exhaustive – they pursued second, third, and fourth opinions from different health care providers, friends, family, or online sources.

[My husband’s] more trusting than me – if the doctor says it’s okay, then it’s okay. I’m more like “Well, we’re going to ask 600 more people. Then we’re going to decide.” – Stacy, third trimester, taking antidepressants

Interestingly, there were a few participants who recognized in advance that information seeking online had the potential to cause them anxiety. These women consciously chose to avoid online searching, and instead consulted a health care provider at the very beginning of their DM process.

That was one time I did not do reading. It’s not my field of expertise and I didn’t want to muddle my mind with information and research that I knew nothing about, so that was one time where it was like, “ok, just give me the facts and let’s figure it out”. – Gail, third trimester, taking antidepressants

Participants also sought information extensively when they deemed the information they had accessed to be insufficient for making a decision. Many participants described explicitly the tremendous responsibility that they felt at the prospect of becoming a mother (page 68), and that this sense of moral or ethical obligation spurred them to pursue information seeking to a greater depth than when making treatment decisions only for themselves.

Really, what it comes down to... this is very focused on him and not so much on me. I probably would have been a lot more relaxed... or less concerned, or there wouldn’t have been that sense of urgency, or the depth of investigation that I would have gone to if it had been me, because yeah, it’s just me. I think that’s probably the big difference, you know, and a huge factor in this - he’s living in my body right now. – Hazel, third trimester, taking antidepressants

Some participants felt that the information they had was insufficient because they were looking for a greater level of informational detail than they had been able to access. This
occurred for some women when they received only a physician’s clinical opinion, without supporting information, in an example of the influence of patriarchy in healthcare on seeking information (page 64). Additionally, some participants commented on finding insufficient detail in terms of information online. For example, Sofia had found information about other women’s experiences of deciding whether to take antidepressants during pregnancy through blogs or online forums, but wasn’t satisfied with the detail included in terms of the baby’s health when mothers had either taken antidepressants or had untreated depression during pregnancy.

I’ve done my research, but I’ve found blogs or question pages where somebody asks a question and a bunch of people comment, and I have found women who are pregnant and taken the antidepressants. I’ve found women who are like, ‘No, I would not take that risk.’ I’ve found women who are pregnant and then they get depressed and then they get put on antidepressants, which then I’m like, that might also happen. Is there a safe route? And the people are like, ‘I took them, I had the baby.’ But there’s not enough information. I was like, ‘but…. did they test the baby?’ There’s also not information telling you what might happen to the baby. – Sofia, preconception, undecided

Finally, extensive information seeking was employed by participants as a strategy to manage conflicts that arose between information, beliefs, and/or preferences (page 123).

Cluster 2: Making sense of information

Making sense of information is another of the three clusters of DM activities (represented by the smaller gray circles in Figure 2.1 on page 59) within the DM process (represented by the blue circle in Figure 2.1 on page 59). This cluster is highlighted in red in Figure 2.5.
**Figure 2.5.** Theoretical model of decision making (DM) about mental health care in relation to pregnancy, with red font highlighting the ‘Making sense of information’ cluster of DM activities, within the DM process.

This cluster of DM activities is intimately entwined with the seeking information cluster. Participants moved back and forth iteratively between seeking information and making sense of information. Activities included in this cluster – that share the goal of making sense of information – are: appraising information for its trustworthiness; reflecting on beliefs; engaging in thought experiments; exploring ways to see the information from different angles; and integrating information to evaluate risks of harm.
Appraising information for trustworthiness

The biggest factor that influenced participants’ appraisal of the trustworthiness of information was its source. Characteristics of the information source that influenced evaluations of its trustworthiness included: symbols of reputability; perceptions of bias or underlying motivations; and the quality of the relationship and informational interaction (when receiving information from a friend, family member, or health care provider). Participants’ confidence in their ability to appraise information for trustworthiness varied; those with educational privilege had the greatest confidence (page 75).

Symbols of reputability

Trustworthiness of information from physicians, friends or family with training in health and/or research, or online sources was judged by most participants on the basis of: claims to expertise; and affiliations with reputable institutions. These factors were equally relevant when women were seeking information about risk of harm to themselves and to their baby. Claims to expertise included: 1) credentials (e.g., physicians were most likely to be considered ‘experts’); 2) specialist training; and 3) number of years of experience. Individuals with specialist training were believed to have up-to-date knowledge from their increased access to the latest research evidence, which participants judged to be more trustworthy. Number of years of experience – a fairly common heuristic symbolizing expertise – was particularly relevant to participants in this context because many were interested in the anecdotal experiences of other women. The number of years a health care provider had practiced was associated with the number of women for whom they had cared, and thus, providers with more years of experience were often deemed to have information that was more trustworthy. Additionally, participants were more likely to trust information from sources (individuals or online) that were affiliated with institutions (usually
hospitals or universities) that were considered reputable. The following quote from Sherry illustrates the influence of all of these symbols of reputability on her appraisal of the trustworthiness of the information she received.

There wasn’t any studies on my particular brand [of antidepressants] with babies and so I was like, “I don’t like that there’s no long-term studies.” We talked for like a second - my doctor and I - about maybe switching or something like that and she was like, “I don’t want to switch you.” She basically kind of laid it out and put it in a framework like how I normally think of things. [...] “You’re just going to have to trust the fact that I’ve been in practice for 30 years.” [...] It kind of really did hit me in a good place when she was saying her personal experience. That’s somebody real life, one on one. It’s like somebody can’t make that shit up. The website, like, it’s not real life, so she knows, she’s more into it than most. She’s an OBGYN and works at one of the great hospitals for women. Yeah so I was like I’m just going to have to trust her and she knows best. I mean she deals with women in full blown labour almost every weekend, right? I think she’s seen the battlefront. She’s the Sherpa on Mt. Everest. – Sherry, preconception, planning to take antidepressants

Perceptions of bias

Most participants were skeptical of information they accessed online. In particular, stories from strangers on online blogs or forums were perceived by most women as being inherently biased towards the negative:

The bad thing is I’m a Googler. [...] It’s other people’s experiences, and what they’ve gone through, and it’s usually never good on the Internet. You’re only going to go on there to write something bad. [...] like, “This is why I think my kid has autism, this is why this happened, this happened...” – Desiree, preconception, undecided

While some participants recognized that information in news articles was likely to be ‘sensationalized’, others weren’t able to disregard this information until they had consulted with a health care provider (page 84). A few participants identified the importance of appraising even scientific articles – generally perceived to be reputable – for the possibility of bias. For example, Hazel (with a PhD in Psychology) discussed the importance of thinking critically about the research data that she was accessing online, including potential conflicts of interests that may have influenced the results.
Critical thinking is the important... I was very cognisant of, you know, what am I reading? where am I getting this from? what does the population look like? So that was very helpful to me, to have that understanding of, okay, you can't just read this and take it, you know, because Pfizer sent it out, and …” – Hazel, third trimester, taking antidepressants

Quality of relationship/interaction

In the majority of cases, if participants sought information from a friend or family member about their perspectives of the risk of harm to the participant’s mental health in the context of depression treatment DM in pregnancy, they were doing so because they trusted that person, and felt that any information provided had high trustworthiness. For example, Farha trusted her mother deeply and wanted her mother’s input on how to manage her mental health during pregnancy.

We've been trying to figure out pregnancy, and so me and my husband have been talking, and coming over to my parents' house, and getting my mom's opinion, because we really wanted to know what she thought, too, of what we have been told... especially because she knew my health before I was taking some of my depression medications. – Farha, preconception, undecided

In terms of risks of harm to a baby, all participants who asked friends/family with training in health and/or research about this did so because they perceived that these friends/family would not only have increased access to reputable information, but that they would be more likely to share the information with them honestly. In addition, women expressed that they could more easily trust interpretations of this information from friends/family because they were acting within the bounds of their relationship – in which the friends/family are personally invested, and not under professional obligations or restrictions. For example, Sofia’s friend worked as a health care provider with a population of women who took Methadone and antidepressants during pregnancy, and she shared with Sofia about how advice about substance and medication use during pregnancy hinges on risk management. In the setting in which this
friend worked, the focus was on harm reduction and risk minimization, where it’s better for babies to be exposed to Methadone and antidepressants than to heroin, maternal overdose, or other risks that go along with heroin use. Sofia asked her friend what she knew about antidepressant use in pregnancy more generally, and trusted that she would share her insider knowledge honestly.

For me, that was really … ‘cause this is her talking, this is not somebody talking from like, ‘oh I need to say this, ‘cause this is what the agenda says’. This was somebody just like … opening her mind, just like what happens behind the stage, right? And so I was like, “Oh my God! So what do you know about antidepressants and pregnancy?”’ And she said, “Well… there is not enough research to tell us what exactly will happen to the baby. Nobody really knows … there’s no research to be like, for sure these bad things are gonna happen or, for sure your baby is gonna be safe”. And she’s like, “now we have some babies that have been born while the mom was taking that medication, but nobody has followed up to see where those babies are 8, 10, 20 years later… if their brain development is fine, if everything else is fine.” – Sofia, preconception, undecided

Level of trust in physicians varied based on the quality of the connection between the women and their physicians. This was the case whether participants were seeking information about risks to themselves or risks to a baby. The quality of the patient-physician connection was influenced by: 1) how frank the physician was perceived to be in disclosing information and answering women’s questions; 2) the extent to which the physician tailored the information to the woman’s situation; and 3) how much the physician supported the woman to make her own choice. Physicians who appeared to be frank in their approach - who didn’t shy away from difficult conversations - more often earned women’s trust.

I know what I’m talking about and I think she respects that a lot. And I have a good rapport with her and vice versa. We can talk very candidly about things. – Stephanie, third trimester, not taking antidepressants

In addition, the more physicians were able to tailor information to the participant, the greater the participants’ trust in the information provided.
The [reproductive psychiatrist] that I’m dealing with really, really understands what is bothering me. So for example, being maybe bipolar, she could’ve put me on an antidepressant and suggested that, but I was happy that she could recognize that my main issue, or where things all go wrong, is when I have my manic episodes, so she felt that I would be better off with the antipsychotic. And that made me feel understood. – Tara, *third trimester, not taking antidepressants*

Finally, participants’ trust in physicians was enhanced when physicians created an environment in which the women felt supported in their DM. For example, Nadia’s reproductive psychiatrist cultivated her trust by providing information in a non-judgmental way to support her in making her own decision. In stark contrast, Nadia’s family doctor undermined trust in their relationship when she was unsupportive in response to Nadia’s information seeking – both practically, in providing no information, and emotionally.

I remember when I was telling [my family doctor] that my husband and I were planning on having a baby, and that I was on this antidepressant and I was concerned about, you know, I didn’t really know, other than what I had researched on the internet, the risks of being on an antidepressant. I remember she said, “well, I wouldn’t want to be on it, but it’s probably okay”. And I remember feeling like, what else do you say? So… that was a negative experience because I felt like she was very judgmental and didn’t offer any solutions. [...] The [reproductive psychiatrist] was really, really good in terms of presenting the information in a very unbiased way and no real preference about what option I wanted to choose. She definitely made it clear that it was my choice, and she was very honest about the risks, the minor risks, that are associated with the antidepressants, and the risks of being depressed while having a baby. It was a very positive session, and I came away with a lot of information, and I felt really empowered by that initial appointment that I had with her. – Nadia, *third trimester, taking antidepressants*

**Confidence in appraising information for trustworthiness**

Most participants were aware that information available online differs in terms of quality – usually characterizing information on blogs and forums as the least trustworthy and information that has been generated or reviewed by experts as most trustworthy. However, some women commented that they lacked confidence in discriminating information of poor quality from information of high quality.
Unfortunately, the internet is full of good and bad information, and Google searches will lead you to both good and bad information, and I probably read equal amounts of reputable information from scientific publications, to forums about antidepressants causing autism and all that kind of stuff. So, I did general internet searches and, you know, not being a scientist, it’s hard to really know what to believe, right? – Nadia, third trimester, taking antidepressants

In contrast, participants with educational privilege were more confident in their ability to filter information accessible online for its trustworthiness (page 75).

**Reflecting on beliefs**

**Medication beliefs**

Participants’ past experiences with antidepressants strongly influenced their attitudes towards continuing, or returning to taking, antidepressants during pregnancy, and their estimation of the likelihood that taking antidepressants would lower their risk for depression.

Participants considered their beliefs regarding medication effectiveness and medication necessity during DM about antidepressants during pregnancy.

**Medication effectiveness**

Many participants, like Madison, felt that antidepressants had been highly effective for them.

Before the medication, I was like that. Some days I would wake up sad and depressed, some days I’d wake up anxious, and some days I’d wake up angry. There wasn’t a lot of happiness there. As soon as I’d open up my eyes, I would just feel anything but happiness. I remember the first morning I woke up and I felt just happy. I thought, “Holy crap, this is what it’s supposed to feel like to actually be happy with your life!” And I thought - I don’t want to stop taking [these antidepressants]. I felt like that for so long that it just kind of came natural and it felt normal to me. Like, I knew it wasn’t, and I didn’t want to feel that way, but I know now that I didn’t know what it was like to wake up and genuinely be happy. I did have side effects, but all I knew is I was happy. Give me whatever side effect you want at this point; I’m finally happy! - Madison, third trimester, not taking antidepressants
Medication necessity beliefs played a pivotal role in DM for these women. For women who didn’t feel that they derived much benefit from antidepressants, but who didn’t experience severe side effects, beliefs about medication effectiveness were more mixed. While Audrey wasn’t convinced that antidepressants were effective for her, she felt reassured that she hadn’t experienced any negative consequences from taking them in the past, and so was willing to give them a try again, seeing their potential benefit to her mental health in pregnancy.

It might be more familiar, like, the fact that I tried a medication once, and even though it didn’t help, it wasn’t a negative experience, so I was more willing to try something this time. – Audrey, third trimester, taking antidepressants

Rachel was ambivalent – believing that antidepressants helped her, but only in a limited way, and would thus have minimal benefit in the perinatal period.

I wouldn’t say [my experience with the different antidepressants I’ve tried has been] overly positive. They just kind of make things borderline normal again. […] I’ve gone back and forth talking about that to [my family doctor], about possibly going back on [antidepressants during pregnancy]. – Rachel, third trimester, not taking antidepressants

Elizabeth, for example, did not believe antidepressants were efficacious for her, and so didn’t believe that they would be helpful in reducing her risk for perinatal depression.

I was adamant that I wasn’t going to take any pills [when my reproductive psychiatrist brought up the] possibility that she would prescribe antidepressants for me. I knew that I just didn’t want to take them and that was the end of that, really. Like, I’ve taken them before, right? So I don’t … didn’t have a good, you know, outcome with it, so I didn’t think any further. – Elizabeth, second trimester, not taking antidepressants

A minority of participants experienced severe side effects with antidepressants and did not find them to be very helpful in managing their depression symptoms. These women did not believe antidepressants were effective for them, nor would be helpful in lowering their risk for perinatal depression.

I'm probably going to take my IUD out next month, because I'll be completely off Cymbalta and that's sort of all coinciding together. If the Cymbalta had not produced the side effects or I felt like it was really working for me, then, yeah, I would have stayed on.
But right now, because of the way that all these factors have kind of collided, I think the idea is to stay off an antidepressant for now and then we could revisit that in the future. – Lena, preconception, undecided

Medication necessity

Participants with a belief in antidepressant effectiveness (whether that belief was strong or weak) had usually questioned – at some point in their history - whether antidepressants were necessary for them to stay mentally healthy. The typical response to this question was to conduct a ‘physical experiment’ in which they either stopped the medication or lowered the dose they were taking, and then closely monitored any ensuing changes in their mental health. These ‘physical experiments’ either solidified or undermined women’s necessity beliefs regarding antidepressants. Most women noticed that their mental health deteriorated as a result of the physical experiment, and this strengthened their medication necessity belief.

I guess because I thought I was dealing okay and things seemed like they were under control. I never thought I was going to be on [the antidepressant] long term, you know what I mean? I guess it was, kind of, an experiment, in a way, to see what would happen, and having never been through this whole thing before, what would happen if I stopped taking it? So I just weaned myself off, and I was okay for a few months but then, over time, I started to get those feelings again and realised, like right away, no, I probably need to go back onto something. – Sarah, second trimester, taking antidepressants

On the other hand, a few participants perceived no change in their mental health (or an improvement in their mental health) following the physical experiment, and this undermined their medication necessity belief.

I was a little nervous going off of Cipralex because I was afraid, you know, even though I was feeling great most of the – like, all of the time - and I felt like I was back to my normal self, but... so I was like “well, if I stop, then am I going to go backwards, and am I going to have - you know, am I going to have a...?” , and thankfully that didn't happen and everything was fine. – Sierra, second trimester, not taking antidepressants

When deciding how to manage their mental health during pregnancy, most participants reflected on the results of past ‘physical experiments’, and many also conducted these tests
during preconception or pregnancy. When conducting ‘physical experiments’ with a focus on pregnancy, most women were engaged in ‘negotiating’ as a strategy to manage conflicting internal beliefs: a medication necessity belief and a belief that taking medication during pregnancy is harmful to a baby (page 129).

Illness beliefs

Participants’ causal attributions for their mental illness varied in terms of the role they believed biological factors played. Frequently, if women believed that mental illness was a weakness or personal failing, they also believed that they ‘should’ be able to manage without medications. This seemed to be associated with self-stigma regarding their mental illness.

I would just rather, you know, go through everything else that I can do, and go to counselling and go … do whatever I can, rather than just take … yeah, pill to feel better. […] there’s a stigma, right? [If] you need to be on antidepressants, then you can’t cope on your own, and you’re not strong enough... and you have to rely on these things. – Elizabeth, second trimester, not taking antidepressants

Many participants made a connection between taking antidepressants and improved mental health through conducting a ‘physical experiment’. This connection typically challenged – at least to some extent – participants’ beliefs that their mental illness was due to their own weakness, and strengthened their belief in biological causes of their depression. This also went along with a stronger antidepressant effectiveness belief.

I thought I was going to feel like I felt on the antidepressants because I was strong now and I was fine. Maybe if it wasn’t in my brain I would be fine. But unfortunately, I’m not fine. So, didn’t work out so well for me. – Desiree, preconception, undecided

Some women still had trouble accepting that taking antidepressants wasn’t a sign of failure, and resisted the idea of taking them for the rest of their lives. For example, even though Molly had seen from physical experiments that antidepressants helped her mental health, and she tried to
accept that there is a biological component to her illness, she expressed a lot of self-stigma and held on to the goal of someday stopping her antidepressants.

Eventually I'd love to be drug-free and that's a goal, but not, you know, that's a future goal, because right now they are keeping me stable. So, I'm really trying not to judge myself too much for being on these meds, and just always think I have something that, oh I just want to be, yeah, I want to be free of them, but because of depression, so it kind of, it sucks. I guess, it's my own hang-ups about them. I just feel like if I'm on medication for anxiety and depression, that means that I am a depressed and anxious person. [...] I mean, in my rational brain, I know that they help me, and there's no problem being on them right now... that if they're working, they're working, and that's what I should care about. But it is, yeah it is definitely what they represent to me that [makes me] judge myself and kind of get hard on myself for still being on them. [...] I’m kind of thinking that maybe, because I’m so, you know, I’m doing so well, maybe it is in part, it’s because of the medication. And I, that’s what I believe now is that it, it’s the combination of me, I’m actually in a really good place in my life... and also that these meds are doing something to stabilize, you know, all the chemicals in my brain.” – Molly, third trimester, taking antidepressants

**Thought experiments: The “what if...” invasion**

Thought experiments were a form of fantasizing that some participants employed when they were trying to make sense of information. In these fantasies, women who were considering taking antidepressants during pregnancy, or who were already taking antidepressants during pregnancy, imagined possible harms that their baby could experience. Almost universally, women expected that they would attribute the harm to their baby to antidepressant use, and anticipated guilt as a result. While this often triggered reassurance seeking (mostly from health care providers), most participants found it difficult to accept reassurance that they received. This occurred more prominently, although not exclusively, in the preconception period, and amongst women with anxiety.

The thought experiments women described in the preconception phase were more often catastrophic in nature – including both short- and long-term outcomes, as well as general and specific concerns.
I just kept saying, like, how will I feel if something happens? Like, is this going to wreck me? That’s the thing is, like, obviously I already have mental health issues, is this going to just exacerbate this thing where I finally... you know, my child has autism and now I blame myself for the rest of my life? [...] You’re going to continue to judge yourself long after the baby is born, as the baby grows... and everything that might be wrong with it, you’re going to start to question, and I think that’s what I was really wrestling with... Is this going to kill me in 20 years if something is really... am I just going to hold onto this idea that I did this, you know? – Samantha, preconception, planning to take antidepressants

In contrast, the thought experiments of participants who were pregnant were more likely to be nagging doubts of smaller magnitude.

[I have had] very small [doubts]. Just like the back of my head going, “What if they don't know yet... they don't know about this medication yet? They’re going to find something... The babies need to be 45, and then they'll find the thing, you know?” [...] I know there’s always a possibility that something . . . I might think whatever it is, is the medication. – Stacy, third trimester, taking antidepressants

Participants who engaged in thought experiments when they were pregnant were likely to seek reassurance repeatedly from health care providers, but to have difficulty accepting the reassurance that they received – as was Nadia’s experience.

It’s definitely more about the consequences for the baby, and that was my ultimate concern. Whether the baby was born healthy without any holes in its heart, or something that would happen later on in the baby’s life that I would look back on and think I caused that because I was on antidepressants, and just feeling like I’ll always hold myself responsible for anything that happens to the baby because I’ll ultimately tell myself that it was because I stayed on antidepressants this has happened. [...] I’ve definitely talked a lot about it with my family and my doctors and it’s helpful, but I still... I think it’s still something in the back of my mind that I’m just holding onto a bit. – Nadia, third trimester, taking antidepressants

Participants were also much more likely to conduct thought experiments during pregnancy if they had an anxiety disorder, and were currently experiencing anxiety symptoms. Jane explicitly pointed out the connection between thought experiments and her experience of anxiety.

Of course, there’s times where I think, “Oh no, I’m taking Paxil... what if our baby does have one of those defects, and dies, and like...? But more so, I was going down those roads before I made the decision to be on them, and trying to conceive. [...] I can imagine regretting the decision if there is a serious complication, and that was one of the listed
side effects. So, I can imagine being, “I should not have taken these drugs.” I think guilt would be a huge thing that I would have to work through. I guess I would hope I would come to a place where I could say to myself, “You made the best decision you could in that moment”. That’s a hard thing for an anxiety-prone person, because I tend to be always thinking about the future, and always thinking about the what-ifs. – Jane, second trimester, taking antidepressants

Anxiety was not only associated with a greater frequency of thought experiments, but also as a consequence of thought experiments. A popular method amongst participants to counter-act the anxiety triggered by thought experiments was to remind themselves of the evidence that the most common harm to a baby as a result of taking antidepressants during pregnancy is neonatal abstinence syndrome, which is transient. Participants were somewhat able to reassure themselves that there was no evidence of long-term harm to a baby from maternal use of antidepressants.

I guess it’s not so bad - as long as there is no permanent damage... that’s my main concern. – Olivia, preconception, undecided

Exploring information from different angles

Additional internal processes that women employed when they were making sense of information were perspective-taking and reframing – both ways of understanding information from different angles.

Perspective-taking

In perspective-taking, participants expanded the time-frame under consideration – looking either backwards in terms of their history and personal experiences of managing their mental health, or looking forwards to put their current decision and prenatal period in the context of the rest of their lives. It was most common for women looking backwards to reflect on how much has changed between now and their previous episode of depression in terms of their coping skills and capacity to manage their mental health. The focus of this exploration was to highlight
reasons why history wouldn’t repeat itself, in response to anxiety about their risk for a depression relapse.

I’ve been to cognitive behavioural therapy for anxiety, depression, and a 20-week program for sexual abuse survivors. So, I have all these coping mechanisms that I can use and I learned a lot of self-talk and stuff like that. So, I use all of that, plus the whole exercise and eating and keeping open with my support people. I mean I still struggle 'cause I'm human, and also there are a lot of hormones going on, which affect things. But I'm very open with it. Whereas before, I would keep it all inside, and I would just worry and worry and worry... and I would isolate myself. But now I talk to my husband a lot, and he lets me cry if I need to, and I just get it out. And then he helps me redirect my thoughts if necessary, and then I'm okay. – Stephanie, third trimester, not taking antidepressants

Another scenario in which participants looked to their past experiences of managing their mental health was when women were speculating about a risk of harm to their baby when they were taking - or considering taking - antidepressants in pregnancy. These women looked to their own experiences with taking antidepressants in an attempt to extrapolate to what their baby could experience.

I’m wondering, because I don’t have a really active baby. You know, I compare myself to other pregnant women and they’re, “Oh my God, she’s always kicking or hurting me or whatever...” and that doesn’t, I haven’t really experienced that. I mean, she moves, you know, quite consistently, so that eases my worries about her. But I’m also thinking, because of the side effects of my medication, I get really sleepy, and I’m wondering if maybe she’s feeling the same side effects, you know? I’m also concerned about her coming off the meds, because when I lower my dosage or have gone off them completely I’ve been pretty crabby and achy, and I’m wondering if I’ll have a little crabby baby, because of that. – Molly, third trimester, taking antidepressants

When some participants looked forwards, they reached the conclusion that the prenatal period is relatively short in the context of their lives, and so it would be worth suffering during that period of time for the sake of their baby’s health.

I went back and forth a lot... but any time that I thought that I came to the decision to go back on it, I would read up on different studies on what it can cause, and what it can do to the baby, and whether that was worth it to make it out another 6 months or another 5 months... [...] And my husband and I talked about it, and there has been times when he said, “You need to go back on it,” and I agreed. And then we would talk about it a day
later or so and we agreed, it’s 9 months, tough it out for that period of time to make sure our baby is safe. – Rachel, third trimester, not taking antidepressants

In contrast, some women reached the conclusion that the perinatal period had the potential to be very long, and that it wouldn’t be worth it to suffer through that time.

I was talking to my partner about it, and we just kept saying, it’s all about quality of life right now, like can you live... because it’s like, this isn’t just a change for right now - this is a few years at least. I can go back on the amitriptyline eventually, but this is all through... I mean, we don’t know if we’re going to get pregnant right away, then there’s the pregnancy, then there’s breastfeeding, and then... So this isn’t just something that I need to make this decision on for... yeah, I can hack this out for a couple months... which is what I kept telling myself, like “No, it’s not worth it to be struggling like this”. – Samantha, preconception, planning to take antidepressants

Reframing

In the process of reframing, participants who had been viewing information through one lens were able to see the same information through a different lens – enabling them to see the information in a new light. For Samantha, this enabled her to redefine what the ‘right’ treatment decision looked like for her.

Definitely for me, it was like the back and forth... I wanted to do it perfect and right, and realizing that this is probably what’s perfect and right for me. – Samantha, preconception, planning to take antidepressants

Participants deciding whether or not to take antidepressants in pregnancy typically framed their decision as a comparison between a potential risk of harm to a baby (taking antidepressants) and a potential risk of harm to themselves (not taking antidepressants). It was very powerful for some women, however, to reframe their decision to accommodate another possibility – that not taking antidepressants could have the potential to harm a baby.

My girlfriend, the doctor, she explained it to me really well. She’s like, the cortisol and all those things are going to hurt the baby more than the antidepressants. And I never thought of that and even [my boyfriend], he didn’t think of that. His thoughts were like no meds, but no - if there’s something going on with me, I’m not crying because I broke a nail. Something is up. And if that’s the case, then you’re going to hurt the baby. Your blood pressure’s going to hurt the baby. So I’m going to take the risk [of taking
antidepressants] and I think I would be okay with taking it... my views have changed. – Desiree, preconception, undecided

Integrating information to evaluate risks of harm

As one participant, Carolyn, who was highly numerically literate observed, evaluating risk is very complex and involves an assessment of not only the likelihood of a given event, but of the perceived magnitude of that outcome.

With my job being in medical devices, I deal with risk a lot, so you do realize how small the risks actually are when you start looking at that stuff. So, I do look at the numbers, I do weigh that, to some degree, and I also look at the severity as well, like how disruptive would that be? Because you could have a really low risk of something really bad happening, or you could have a high risk of something not so bad happening [laughs]. So, you really have to consider both the risk and the severity. – Carolyn, third trimester, taking antidepressants

Amongst participants in general, however, numeracy levels were fairly low, and women often didn’t remember numbers that they came across while seeking information.

I don’t remember any numbers, just kind of what the risks were or side effects. I was just scared of having the baby have jitters and stuff like that. I just didn't want to be on any medication while pregnant. I didn't want any of the side effects to affect the fetus, I guess, or the baby. – Linda, third trimester, not taking antidepressants

Even participants who were more cognizant of numerical risk and tried to process the statistics, commented on their difficulty in avoiding black-and-white thinking, and their tendency to artificially inflate risk by assuming that the outcome – no matter how objectively infrequent – would happen to them. The fact that there was even a possibility of harm to a baby – no matter how marginal - as a result of taking antidepressants during pregnancy, was judged by many participants to be too high a risk.

The numbers are reassuring for sure, and it’s something that I do try and focus on because that’s the rational thing to do, but I do have this tendency to feel like if there’s a potential for something bad to happen, it’s going to happen to me, which is... it’s not a good way to think, so I try - I really do try - and focus on the statistics, and the real likelihood, but it’s easy to fall into the trap of thinking, “why wouldn’t it happen to me?”
So yeah, it is reassuring and I try to focus on that, but then your mind will kind of play games with you. – Nadia, third trimester, taking antidepressants

Evaluating risk of harm to self

The majority of participants believed that they had a high baseline risk for perinatal depression. These women perceived that their risk for perinatal depression was high not only as a result of their history of depression, but also because of the belief that pregnancy itself – with all its hormonal changes - is a stressor that will increase the likelihood of depression.

I’m very sensitive to hormonal changes. My depression and anxiety always got worse right before my periods. It seemed to be linked to hormones. So, I think before getting pregnant, I felt like more in control, like I could control things. I knew when my period was coming, I knew when, you know, I could kind of – it felt like I had a bit of control, with like meditation, and journaling, and medication, and exercise, and like counselling, and all these things. I could keep it – my mood stable. Going into pregnancy was quite scary. It took me a long time to decide to do it, because I knew that I was at an increased risk for post-partum depression, pre-partum... whatever-the-period-is-when-you’re-pregnant depression. So, it was quite scary. – Jane, second trimester, taking antidepressants

Another factor that elevated participants’ perception of the risk of a depression relapse in the perinatal period was when they had an older child. These participants perceived the impact of depression as having greater consequences when they considered not only their baby but also their older child.

I think the last time, it was like not being able to get out of bed, as well as not being able to get out of my head. Maybe it was when I was feeling a lot of anxiety or something. It was just like, I couldn’t think myself out of it. And like distraction wasn’t really helping, just like nothing was really helping. And because I have a toddler to take care of, the consequences are more dire. – Natsumi, second trimester, not taking antidepressants

There were two ways by which participants were able to lower their perceived risk of perinatal depression: 1) reflecting on ways in which their capacity to manage their mental health had increased relative to their past experience(s) (page 102); and 2) reflecting on a safety net they had built/were building (page 116).
Evaluating risk of harm to a baby

A prevalent belief that was very influential in DM about depression treatment during pregnancy was the belief that taking any medication during pregnancy can be harmful to the developing baby. It was clear from the interviews that this belief stemmed, at least in part, from societal expectations of pregnant women, and associated female gender roles (page 68). It was in the context of this belief that participants sought and interpreted information about risks of harm to a baby that were specific to antidepressants. Many participants found the information that they accessed regarding risks of harm to a baby due to antidepressant use in pregnancy to be concerning, and evaluated these risks to be high.

I know with the heart defects there was actually a percentage listed based on the participants. And I know… I’m almost 100% sure that it was above 10%. Which was very high for me and my decision making. So yes, there were percentages, there was also definitely high/low/medium. Ultimately there was enough that I chose not to continue. – Rachel, third trimester, not taking antidepressants

Participants were particularly likely to perceive the risk(s) of harm to a baby due to antidepressant use in pregnancy as high if they engaged in thought experiments (page 100). Risk perception was also elevated when the word ‘withdrawal’ was used in the context of neonatal abstinence syndrome amongst babies whose mothers were taking antidepressants during pregnancy.

[My reproductive psychiatrist] was saying some babies get the jitters. I’m like, “Oh god!” You don’t want to think of your baby coming out like a heroin addict baby. That’s the sad part because you’re like – that sucks. When I think of it that way, it sucks. – Desiree, preconception, undecided

A few participants were able to reframe their expectations around ‘withdrawal’ by getting more detail in terms of what that means, in concrete terms. This translation from a daunting umbrella term into what a mother might actually see helped to lower women’s perceptions of the risk of ‘withdrawal’ to their baby.
That seemed to be the base thing they had to say about it, and that they had followed kids on this medication up to certain years, and haven't seen anything outside the baseline. And it was like, “Well, if my baby’s more jittery and crying for the first few weeks, how would I know the difference?” – Stacy, third trimester, taking antidepressants

Even if participants hadn’t found any information indicating specific risks of harm to a baby related to taking an antidepressant during pregnancy, or judged the risks they had found to be objectively low, quite a few participants were still fearful and held onto their initial belief that medication use during pregnancy is likely to be harmful to a baby. These participants didn’t feel that there was enough reassuring information available to confirm that their baby wouldn’t be harmed by the use of antidepressants during pregnancy.

My husband seems a lot more comfortable with it, just because he … he's more of a numbers person and he heard it and he was just like well, I feel like it's not that bad, but for me, I'm just like well, when we look at it all together, you don't know what's going to happen when you're outside the medications, adding up, what's done to a baby. So for me it was a worry, for him … he was just like well, the percentage of that is so low, I feel like it might not be … like, the risk is not that high... [but for me] it's just the unknown...

– Farha, preconception, undecided

In contrast, a minority of women explicitly stated that they saw the lack of evidence of harm (even in the context of uncertainty in terms of outcomes) as reassuring. These women perceived that antidepressants are really commonly used, and have been for many years, and they felt that any major consequences in terms of harms to babies as a result of mothers taking antidepressants during pregnancy would have surfaced already.

I usually like numbers; I haven’t been as fastidious as I usually am. I usually like going through the research, and seeing actual methodology, and what they did, and what the sample size was, and how long they followed the kids, but I’ve also realized that I think that people have been on antidepressants long enough that it’s not a new trial. Like, there was that one medication where, remember, things went upside down, and a whole bunch of kids ended up getting, I don’t remember what it was called, but there was something that happened a long time ago, it was a new medication that some mothers took, but it all happened I think within the first year or two of the medication being out, and so these have all been out long enough that there’s nothing that they’ve seen so far. – Audrey, third trimester, taking antidepressants
Some participants were able to lower their risk perception with the dual beliefs that they were taking a low antidepressant dose, and that a lower dose carries with it lower risk.

I was on such a low dosage that it was, you know, definitely not going to do anything to baby’s production. – Pamela, started weaning off antidepressant preconception, finished weaning off by end of first trimester

Quite a few participants ultimately reached the conclusion that the risk of harm to a baby from taking antidepressants during pregnancy was quite low. They based this conclusion on the research evidence and/or from stories of other women’s experiences they had read or heard from friends, family members, or health care providers.

I had been thinking in terms of numbers, because I had already actually read all the reports – well, not – I didn’t read the full studies, I read the Motherisk compiled reports. And I think what it was, is that, in my appointment with [my reproductive psychiatrist], just the way she was talking seemed a lot more – like, again, she never told me what to do... it was very much informed consent. But the way she said it, I guess, she gave more information. Like she said that with Paxil, there’s been two really good studies that show – one showed no increased risk, one showed... and I may be getting facts wrong, but it was something like this... one showed no increased risk, and one showed like a very small – like half a percent increased risk. And then there were two not very good studies that showed perhaps slightly higher risks, but they weren’t done as well. And she said like, “Yeah, I have tons of women taking these, I fully support you staying on them, or I would support you trying this.” – Jane, second trimester, taking antidepressants

Cluster 3: Self-soothing

Self-soothing is another of the three clusters of DM activities (represented by the smaller gray circles in Figure 2.1 on page 59) within the DM process (represented by the blue circle in Figure 2.1 on page 59). This cluster is highlighted in red in Figure 2.6.
Figure 2.6. Theoretical model of decision making (DM) about mental health care in relation to pregnancy, with red font highlighting the ‘Self-soothing’ cluster of DM activities, within the DM process.

I look at the information I get, and it’s about what I'm comfortable with, and what makes sense to me. [...] No doctor told me of any like extreme circumstance beyond the baseline, so I . . . that’s what helped me make the decision. [...] It was just about getting the information that they know about and feeling comfortable with it.” – Stacy, third trimester, taking antidepressants

Participants talked about the need to ‘get comfortable’ as part of the DM process. Women moved back and forth between ‘seeking information’ or ‘making sense of information’ and ‘self-soothing’. Movement to the ‘self-soothing’ cluster was triggered by the fear, anxiety, and/or guilt that women encountered in the DM process. Participants sought comfort in response to these negative emotions by: repeating a mantra; normalizing; gatekeeping; and/or building a safety net. It was common for women who chose to take antidepressants during pregnancy to invest a lot of
time in preconception DM, and to rely heavily on self-soothing during this DM period. Women who chose not to take antidepressants in pregnancy were more likely to stop their antidepressants when they found out they were pregnant and more likely to engage in self-soothing if their symptoms of mental illness returned.

Repeating a mantra

Mantras were words or phrases that participants repeated as a form of self-affirmation. They were used when women were feeling insecure about their decision or the process, in an attempt to reassure themselves and put the brakes on escalating anxiety or catastrophic thinking. Mantras women employed included: “doing what I need to do”, “healthy mom = healthy baby”, and “doing the best I can”. Mantras did not always succeed in fending off catastrophic thinking, and some women – particularly those with co-morbid anxiety disorders – identified a need to escalate beyond the use of mantras to consciously choose to let the decision go (page 138).

Most participants who took antidepressants during pregnancy used a mantra centering around “doing what I need to do”. This helped women to focus on their medication necessity belief and its importance in their DM process. Some of the power of framing a decision as necessary was in combatting feelings of guilt or anticipatory guilt, or – alternatively – in assuaging anxiety.

I’ve definitely felt – continue to feel - good about it. Obviously, I don't want the baby to have any adverse effects because of it, and so I'm a little nervous that she might . . . have a low APGAR or whatever, but I think . . . No, it was what I needed to do. I think it improves health outcomes for both of us, overall, in such a way that it hasn’t really come up for me. – Whitney, third trimester, taking antidepressants

One extreme manifestation of this framing of the decision to take antidepressants during pregnancy as necessary occurred for one participant, Molly, who expressed that she didn’t have a choice because stopping antidepressants was not an option for her at that time.
I feel like I haven’t really had the opportunity to make a decision about taking them. Like, right now it's not an option to come off the meds or to lower my dose. Because I know the harmful effect to my own mental health when I do from past experience, like when I'm not pregnant. So, yeah, I haven’t really felt like I have an option... there is no other option, but to stay on these meds. That’s what the doctor said too, like, if I'm doing well, then that’s more important than trying to be drug-free at the moment. And because the baby's doing well, and there is no significant evidence that these meds harm the baby, that's just the best option for me. Yeah, I haven’t felt like I've had an option. – Molly, third trimester, taking antidepressants

Some participants who took antidepressants during pregnancy used the mantra “healthy mom = healthy baby”. This mantra arose from the corresponding belief that – for a baby to be healthy, the baby’s mom needs to be healthy, and was a corollary to a woman’s medication necessity belief.

If I can’t take care of me, and I’m not emotionally available, I can’t take care of a baby. – Gail, third trimester, taking antidepressants

Many participants used another mantra focused on “doing the best I can”. This mantra was used by participants across decision categories – taking antidepressants, not taking antidepressants, and undecided. Participants used this mantra to try to make peace with the limits of what they could control in the situation they were facing. This strategy helped women to be kind to themselves and promoted acceptance of their chosen treatment strategy (if they had made a decision).

I have had a couple of those thoughts... “What if it's really, really bad? What if I have postpartum depression and I can't attach properly to my kid? What if...”... you know, sort of like going down the bad path. And I'm just trying to stop myself from that and be like, “Okay, you're preparing yourself, you're going to totally try to do the best that you can”... and not get too wrapped up in those. – Lena, preconception, undecided

While mantras were an attempt by women to reassure themselves, they were not always effective and doubts sometimes crept in. For example, Pamela chose not to take antidepressants during pregnancy, and was relying on other self-management strategies for her mental health (such as social support and self-guided DBT). As symptoms of depression began to return during
her pregnancy, she tried invoking the mantra of doing her best, but she began to question whether that would be enough.

I’m going to just try my best to stay level-minded and just be as positive as I can be. [...] And just trying to like stay positive, but I mean, obviously you can only stay positive for so long (laughs). – Pamela, third trimester, not taking antidepressants

Mantras often were not enough for women with co-morbid anxiety disorders, such as Pamela. Many of these women eventually required a strategy to help them let go of their decision, and fend off catastrophic thinking and the associated overwhelming emotions (page 138).

**Normalizing**

Many participants engaged in a normalizing process when fearful of either judgment (those taking antidepressants or undecided) or despair (those not taking antidepressants or undecided). Women who chose to take antidepressants during pregnancy feared judgment due to stigma (page 71), and used normalizing in an attempt to counteract this stigma. Normalizing worked to counteract stigma by enabling women to see the commonalities between their experience and those of others in a connection to their common humanity, thereby challenging the stigmatizing narrative of ‘other-ness’. Normalizing strategies in this case were either comparing antidepressant use during pregnancy to treatment for other chronic illnesses during pregnancy (like Samantha), or reframing antidepressant use as a common choice, with good outcomes (like Sarah).

From somebody who doesn’t have anything, who doesn’t smoke, drink, or take any kind of drugs that they need, they wouldn’t understand... why in the world wouldn’t you stop taking this drug? [...] But nobody would ever say, “Oh you’re a diabetic - stop taking your needle while you’re pregnant”, like it’s just laughable. – Samantha, preconception, planning to take antidepressants

Society, now, people are always like, “Oh, don't take medication, don't do this...”, but, especially for me, it was a big learning curve that yeah, there is actually a place for it and, you know, it's good to sometimes just take a chance and trust the system, because there's
a reason it's there, and it's worked for so many people, you know what I mean? – Sarah, second trimester, taking antidepressants

Women who chose not to take antidepressants in pregnancy also used normalizing to justify their choice. The trigger prompting normalizing for them, however, was fear of despair. When they noticed symptoms of depression returning, they used normalizing to alleviate anxiety about the possibility of a full relapse. In this context, normalizing worked to support participants’ interpretation of their symptoms as a normal part of pregnancy, rather than a full relapse, thus keeping the information about their symptoms at a distance and allowing them to feel justified in continuing in their choice not to take antidepressants.

There are certain things that trigger it, and everybody has certain triggers that make them anxious. I think right now what I’m experiencing is definitely part of the hormones through pregnancy, that I’m nesting, and things are coming up so quickly, and the expectation, and all my thoughts... like, “Am I going to be this? am I going to be that?” and just not being as mobile and having the freedom, and being kind of, not stuck, but like having to adapt to a new transition of lifestyles. [...] So it’s just, I would say, the transition and yeah, there’s been some definitely hard days where it’s been super depressing and I can’t get out (laughs). And I know it’s not my fault, but it’s something that, you know, is part of the course and it’ll pass, but... – Pamela, third trimester, not taking antidepressants

Gatekeeping: Woman as sentry controlling the drawbridge

Gatekeeping was a self-soothing strategy that most participants employed to manage the potential for, or the experience of, anxiety/fear/guilt resulting from societal judgment of mental illness and antidepressant use in pregnancy (pages 68 and 71). Participants faced a great deal of pressure stemming from societal expectations of pregnant women. For example, they commented on how often people that they knew – and even people with whom they were not acquainted – offered unsolicited advice or stories regarding pregnancy.

You’re inundated with people who haven’t done the research, and don’t understand it, and they want to give you an opinion. [...] Everyone really feels like they have the right to weigh in on another person’s decisions. They really do, especially when it comes to pregnancy, I find that people just... there’s no reservation on giving your thoughts, like
you’re interested in unsolicited advice, you know what I mean? And to think, like, you really think I didn’t actually weigh the pros and cons of this? – Samantha, preconception, planning to take antidepressants

Selective disclosure was a gatekeeping strategy used by most participants – across decision groups (taking antidepressants/ not taking antidepressants/ undecided) - to protect against the potential for judgment. Selective disclosure used by participants ranged from avoiding sharing any information about their mental illness or its management with anyone other than their health care providers, to being cautiously open, depending on their evaluations of whether a person or situation would likely be safe for disclosure.

I haven’t been talking to anyone about this, deliberately. I mean I know, my brother who I love dearly… and he’s not, thank goodness, prone to depression, and he is a very strong-willed, very focused, just, successful individual, he... I remember years ago, when I went on medication, we were both in our early twenties, it kind of upset him a bit. He was saying, “But you don’t need this...” And since then, I haven’t spoken to him about it, and as far as I know, he doesn’t know that I’m on medication. And I certainly wouldn’t speak to him about being pregnant on medication, because it would horrify him that I would risk damaging a child. So... and he’s a highly intelligent, wonderful human being, but there are just certain people who I will not talk to about this. In fact, I probably wouldn’t talk to anyone about this (laughs) unless it’s either my mother, or my partner, or a professional. – Olivia, preconception, undecided

Two additional gatekeeping strategies were used by participants who were taking, or planning to take, antidepressants during pregnancy: 1) keeping emotional distance; and 2) seeking more information from a trusted expert (page 84). These women needed to manage their emotional reactions to judgement of women taking antidepressants in pregnancy that arose either in conversation with acquaintances or in the media. Many of these participants tried to keep their emotional distance to avoid internalizing the stigmatizing message.

I’ve had to kind of filter things out. [...] This whole experience has very much made me have to learn self-trust. I tend to really rely on other people’s... I care a lot what other people think about my decisions, and so this whole experience has been a huge lesson in sticking to my guns, and being confident in my decision. So, it’s been good, because I’ve been like... you can say that to me, I’m not going to let it bug me... I’m not going to let it
affect me, because you don’t know what I know, and you’re not me. – Jane, second trimester, taking antidepressants

Some of these participants tried to keep their emotional distance by re-focusing on supports they had in place and acknowledging the limits of what they could control.

Periodically, there will be studies that appear in the media that will cause me a lot of anxiety... there was one published around Christmas-time, I think out of Quebec, that linked the antidepressants to autism, and I... that will send me down a path of self-doubt and... I feel like I’m vulnerable to other people’s opinions and news stories, which is obviously kind of normal but, yeah, I have to focus on the support that I have, and not on the negative stuff that is out there, because there always will be. – Nadia, third trimester, taking antidepressants

Building a safety net

Building a safety net was a self-soothing strategy that participants used to manage their anxiety and fear regarding a depression relapse. The different approaches women used in building a safety net were practical, proactive ways of gaining a sense of control and security through planning. The most common ways in which women built a safety net were: activating a connection to a trusted health care provider or service; strengthening social support networks; or holding onto antidepressants as a back-up plan.

Activating a connection to a trusted health care provider or service

Most participants, across the three decision categories, took comfort in strengthening their connection(s) to health care providers/services as a concrete step they could take to assuage anxiety/fear regarding a depression relapse. In order to do this, women informed their providers about their pregnancy plans and sought support from providers in the preconception/pregnancy. For some women, this included re-activating a connection to a provider that had supported them in a past pregnancy or depression episode to ensure that their referral was active, should their mental health deteriorate.
I saw [my reproductive psychiatrist] about a month ago to check in. I’d seen her earlier too, when I was first pregnant for the third time, just to check in again and to be on the radar. I wanted my referral to be active so, if I start to go, I can see her right away. – Whitney, third trimester, taking antidepressants

Social support - “It takes a village”

Women were very aware that social support acts as a protective factor for mental health – with the implication that strong social support could lower their risk for perinatal depression. Many participants (across the three decision categories) sought information about the types of support – both practical and emotional – to which they could have access during the perinatal period, and attempted to recruit additional support from their social network. Sources of this information included internal reflection and through conversation with their partner, family, and friends – either learning about others’ experiences through stories of family and friends, or explicitly asking family and friends about their willingness to provide different types of support. Some women also occasionally sought information about the availability of support groups that they could join. Sources of information about support groups included: health care providers, prenatal classes, Google searches, or friends and family.

I met with the reproductive psychiatrist. She gave me such good like, it takes a village to raise a child, and make sure you have this, this and this. And she was so clear that I loved it. And now I’m aware, I was like, so my sister-in-law is going to move back to Vancouver, and I told her I want her to be around, and she’s totally down. And I’ve talked to family, like six months ago or so, I’ve talked to [my husband]’s other sister and mom of how you think you can help. So, the other sister is down for taking the kid for a couple times a week for different activities. Yeah, so I think reproductive psychiatry definitely was the point where it added like, this is possible [to have a baby]. – Najdah, preconception, undecided

Holding onto antidepressants as a back-up plan

The majority of participants who chose not to take antidepressants during pregnancy held onto the option (and in some cases a physical prescription) of antidepressants as a back-up plan.
This safety net functioned for them as something they could fall back on if their depression symptoms returned, or became unbearable.

It’s been quite dramatic changing over the last three months. Last week, I had more tears. [My reproductive psychiatrist] gave me a prescription for the antidepressant already... maybe in case she’s away when I need it... and I already went to the pharmacy to get it... so I have it now as security (gesture of holding onto it)... I can start it right away after delivery if I need it. – *Wakana, third trimester, not taking antidepressants*

**Reaching a decision... or not**

A decision is represented by the white circle with a broken black outline in Figure 2.1 on page 59. Participants engaged in further processes while reaching towards a decision, which are represented by the two black arrows from the ‘Making sense of information’ and ‘Self-soothing’ clusters (gray circles) to the white ‘decision’ circle in Figure 2.1 on page 59. These aspects of the theoretical model are highlighted in red in Figure 2.7.
Figure 2.7. Theoretical model of decision making (DM) about mental health care in relation to pregnancy, with red font highlighting the white ‘decision’ circle representing a decision, if one is reached, and the arrows representing processes used to reach towards a decision.

I feel, in some ways, this is the biggest decision I’ve ever made. It sounds really weird, but it’s like... because you’re obviously directly responsible for this life you’re going to create, and you automatically think like, I want to do everything I can. And so, you feel really weak and you feel a bit like a failure because you’re not able to, you know... [...] I honestly would say this is one of the biggest decisions of my life. Not to just have a child, but to deal with all these medications. It 100% has been; it’s been huge in my life. – Samantha, preconception, planning to take antidepressants

Most participants characterized the decision of how to manage their mental health and their risk of mental illness during pregnancy as very difficult. Not all participants had reached a decision at the time of interview regarding overall depression treatment strategy (to take antidepressants or not) during pregnancy. All participants who were undecided at the time of
interview were preconception. Having said that, some of these participants had reached a
decision to delay the decision regarding depression treatment during pregnancy. A further few
participants were able to easily reach a decision not to take antidepressants, and to feel confident
in their decision. These participants didn’t have any medication necessity belief at the time of
reaching their decision, but their confidence in their decision wavered if symptoms returned,
causing them to question whether they needed to revise their medication necessity belief.
Participants managed the anxiety that this inspired using normalizing (page 113).

Participants’ navigations through the three clusters of activities (pages 77, 89, and 109)
towards reaching decisions included overarching processes for synthesizing information.
Specifically, participants evaluated information for its consistency between sources and
congruence with their beliefs/preferences, managed conflicts, and assigned weight to
information. Most participants navigated the DM activity clusters and synthesizing processes (at
least in part) with either a health care provider or partner (or both). Sharing the DM in this way
helped participants to reach a decision. For some participants who had reached a decision, it was
very important to find ways to accept it. Strategies to accept their decision included: consciously
choosing to let go of the DM process, acknowledging the limits of controllability, and showing
themselves that they had behaved responsibly.

**Synthesizing information: Is it consistent or contradictory, and convergent or discrepant?**

Participants perceived information from different sources regarding depression treatment
in pregnancy to be consistent or contradictory. They also perceived information to be either
convergent or discrepant with their beliefs or preferences. Usually, when participants perceived
that information from different sources was consistent, and convergent with their beliefs and
preferences, they were able to reach a decision more easily and expeditiously. In contrast, when participants perceived information to be contradictory between sources, and/or discrepant with their beliefs or preferences, they needed strategies (and often additional time) to manage (and ideally resolve) this conflict.

**Consistent and convergent**

Some participants perceived all of the information that they received to be consistent across sources – either in line with a decision to take antidepressants during pregnancy, or not to take antidepressants during pregnancy. This was more likely to occur in the preconception or early pregnancy; as women progressed in the pregnancy, they were likely to encounter contradictory information at some point (as they encountered more providers and more/different information; e.g., page 123).

Further, it was evident from the interviews that some participants’ *a priori* beliefs influenced their perception of information such that it was more likely to be perceived as convergent with their beliefs/preferences. This was seen when participants specifically sought validation for their initial preference. Many participants who were already taking antidepressants sought reassurance or confirmation that they could continue to take them in pregnancy.

Honestly, I didn’t want to have to go off of them, because that freaks me out... so I may have gone in with a bias even... I wanted reassurance that this was the right... that this was a good decision to stay on it, because I tried going off Paxil before... [...] when I left the appointment, I left feeling like the [reproductive] psychiatrist is supportive of me staying on these medications, and it’s probably better for me to stay on. [...] if either of those [my mom or husband], particularly my husband, had been like, I think this is a really bad idea, or if the psychiatrist had said like, I really advise that patients don’t do this... but I think because all these things were kind of giving me the same message, plus that was the message I was most inclined to... like, I wanted that to be the case... and the thought of how bad it could be also weighed heavily. So, if they tell me that there’s serious risks of taking antidepressants, then I really do have to consider just suffering through it. But I really hope that it is actually okay, and then it turned out that everything was kind of affirming that decision, or aligning with that. – *Jane, second trimester, taking antidepressants*
Many participants who chose not to take antidepressants during pregnancy also sought validation for their decision from their health care provider, although this occurred less often.

We were concerned about the side effects and stuff, so I think we almost made the decision first, just for what we thought was best, but then we also wanted to make sure that the doctors were okay with that decision, and then the information they gave us was helpful and confirmed [our decision]. – Sierra, second trimester, not taking antidepressants

Another example of information being perceived as convergent with participants’ beliefs/preferences was when participants interpreted research evidence. While most participants expressed that they valued scientific evidence in their DM, the same (supposedly objective) evidence was used by some participants to support a decision not to take antidepressants, and by others to support a decision to take antidepressants. Rachel and Hazel were both taking bupropion in the preconception, and reviewed the available research evidence about taking it during pregnancy. While both heavily emphasized the importance of the research evidence in their DM, Rachel decided to stop taking bupropion during pregnancy, while Hazel decided to continue taking it.

Catriona: Is there one thing that you think has been most influential on deciding to not take antidepressants in pregnancy?

Rachel: Umm... Science? (Laughs). Just studies, and obviously the studies that I’ve read and the studies that my doctor has shared. Just the general research that has been done on different side effects and weighing the pros and cons of that. – Rachel, third trimester, stopped taking bupropion [had not been completely effective for her]

I sort of felt like, if I could just stop taking all this, it would really be ideal, but that’s just not... it wasn’t my reality, and the consequence of trying to do that can be far more dangerous to me and the baby than doing something that, upon investigation of research and data, was telling me that this is probably more in your best interests. – Hazel, third trimester, continued taking bupropion [very effective for her]

A few participants explicitly commented that research evidence is not objective. As a result of this belief, they either disregarded research evidence or approached it with caution.
I don’t believe in studies, to be honest with you, ‘cause they are so foul. The numbers are so deceiving at times, like the way you say it, the way you put it. And you always find studies to either support the argument or not support the argument. What’s the point? So, I like philosophy way more, cause at least they say it’s philosophy. – Najdah, preconception, undecided

Managing conflict: Discordance between information, beliefs, and/or preferences

Many sources of conflict in the DM process were discussed. Participants sometimes perceived: 1) information they received from different sources to be contradictory; 2) information to be discrepant with their beliefs/preferences; 3) their own beliefs/preferences to be in conflict; and/or 4) their beliefs/preferences to be in conflict with those of their provider/partner. These four types of conflicts often occurred concurrently, and strategies for managing them weren’t mutually exclusive; some participants used a combination. Conflict-resolution strategies included:

- seeking more information;
- maintaining distance; and
- negotiating.

Conflict-resolution strategies: Seeking more information

Many participants employed the strategy ‘seeking more information’ when they either faced contradictory information or perceived a discrepancy between the information they accessed and their beliefs/preferences. Participants employing this strategy were those who hadn’t yet decided, or who weren’t confident in their decision. Some participants received contradictory information when they consulted a different health care provider. This was the most common trigger for seeking more information in response to contradictory or discrepant information (from any combination of sources).
I asked my GP, “How safe is it to take this medicine while you’re pregnant?” ‘Cause if I look at the information available, it says that it’s not recommended for pregnant women, that the effects on the fetus are unknown. Which means that it’s like flipping a coin. I said, “What can you tell me about it, is there research that has …?” And he’s like, “Uhhhh, no it’s fine, you can take it, it doesn’t matter.” And I’m like, “But… it says not to…” [...] And then I talked with my gynaecologist in Mexico … now, in Mexico, doctors are a little bit more conservative in their thinking. They’re always gonna be more safe than try to flip the coin or risk it. And he’s known me since I’m 13, right? Since I had my first period. So he knows that I’m on this medication. At that time, I had an IUD, and I asked him to remove it. [...] He was like, “Okay, Sofia, you’re also taking antidepressants…” He was like really stern... imagine it was your grandpa, or your dad, and that’s how he was treating me. And he told me, “Sofia, you have to be really, really careful. You’re gonna have to wear condoms and not do it while you’re fertile because if you get pregnant it could be really dangerous for the baby.” And then I said to him, “Okay, why?” And he explained, “Because you’re on the cipralex and you’re also on the quetiapine- all of this can affect the fetus.” He was like, “You don’t want to take that risk.” He’s like, “So if you ever want to get pregnant, you’re going to have to see a gynaecologist, a psychiatrist, and probably get off the medication.” So then I’m like, okay, Canadian doctors say, “Flip the coin”, and my gynaecologist in Mexico says, “No, no, no, you have to be careful. This is for real. This is a dangerous zone.” So then you’re just left super confused, and I have to be like, okay, do you risk it and stop taking the medication in order to make sure there’s not going to be any effect on the baby? Or, do you take a chance, get pregnant with the medication, and hopefully the baby is gonna be fine? – Sofia, preconception, undecided

Seeking more information was also used by a few participants, like Farha, who perceived that information was discrepant with their beliefs/preferences. Farha had “always thought we weren't ever going to have kids and we could adopt.” She had strongly held beliefs that she couldn’t manage without her antidepressants, but also that taking her antidepressants during pregnancy could be harmful to a developing baby. She repeatedly consulted with different health care providers and family members because the messages she kept receiving conflicted with her beliefs.

That's something that my neurologist said, and that was something [my reproductive psychiatrist] said and … that's easy for them to say, but I don't really feel okay with just trying to conceive and then just getting an abortion afterwards ... Everyone keeps saying, “We don't want you to miss out on motherhood”, and it makes me a little uneasy, because I don't know if they're saying it because they just want to keep my hopes up, or if they don't want to be like, “No, it's not possible”, or what's really actually going on? [...] Now we have most of the information, so now it's just getting another opinion and being like,
do you agree with this opinion, too? Like, from my GP, because obviously we do want a second opinion, and confirming what they think too... I think, maybe once we have the second opinion too, then we know that we have all the information possible, and then we can make a decision from there. – Farha, preconception, undecided

**Conflict-resolution strategies: Maintaining distance**

An alternative strategy used by many participants for managing information that was contradictory and/or discrepant with their beliefs/preferences was to maintain their distance. Distancing tactics included: 1) keeping the information at a distance; and 2) keeping the decision at a distance (i.e., deferring the decision).

**Keeping contradictory/discrepant information at a distance**

Participants did this by avoiding engagement with the contradictory/discrepant information; instead, they put it to one side without giving it much attention. This distancing tactic was employed by some participants when they had already reached a decision, which had been supported by a health care provider, and then received information later in the pregnancy from a different health care provider that conflicted with their decision. Again, contradictory/discrepant information from different health care providers was the most common trigger for keeping the information at a distance (more common than contradictory/discrepant information from friends, or discrepant information from internal reflection on current symptoms – page 113).

I had gone to the walk-in clinic, and the walk-in clinic doctor had told me that there was little information about it, and that it’s possible there’s a small chance that it could have an effect on the baby... he said it was inconclusive, the research or the studies, but I just decided that I didn’t want to… it wasn’t worth it for me to take that chance at that time, because I was feeling alright anyway. [...] [My reproductive psychiatrist] talked to me more about my concerns about [my antidepressant] harming the baby and explained to me more that it’s probably fine... I’m not really convinced it wouldn’t hurt the baby, so I just prefer not to bother with it right now. – Vanessa, second trimester, not taking antidepressants
Keeping the decision at a distance (deferring the decision)

A different strategy that many participants used to manage conflicting beliefs and preferences was to keep the decision at a distance by deferring the decision. This distancing tactic was used in response to internally conflicting beliefs and/or participant preferences that were in conflict with those of their provider/partner/family. Deferring the decision alleviated the pressure and anxiety of making a decision immediately and entailed exiting the DM process with the intention to re-enter another time.

Participants who deferred the decision about how to manage their mental health overall in pregnancy (to take antidepressants or not), did so when they were preconception. They had an unresolved internal conflict between beliefs, and this decision was tied to their DM about trying to conceive a child. This occurred bidirectionally; some women delayed trying to conceive because they weren’t sure how to manage their mental health during pregnancy, while other women took the pressure off deciding how to manage their mental health during pregnancy because they weren’t ready to have a child yet.

Pregnant participants deferred shorter-term decisions – such as whether to increase their dose or resume taking an antidepressant during pregnancy or in the postpartum. For these short-term decisions, participants maintained the status quo and planned to revisit the decision if they exceeded a given threshold of symptom severity, or after a particular length of time (e.g., after the baby’s birth), if that threshold of symptom severity had not been reached by then. In order to determine whether they exceeded their defined threshold of symptom severity, they heightened their vigilance in monitoring their symptoms. Deferring these decisions thus enabled participants to seek more information (mostly through internal reflection) to inform these decisions. All
participants who ultimately increased their antidepressant dose during pregnancy deferred this
decision initially.

About 19 weeks, my mood was deteriorating, and I was starting to get nervous that things
were coming back. And the psychiatrist had said, like, your blood volume has increased,
and so you may need to increase [the dose of your antidepressant]. So, I went to the GP,
and said, like, “I don’t know what to do. Should I increase it? Should I not?” [...] And she
said, “You know, a lot of women start to feel really great around 21 – 22 weeks, so if you
want, you could wait a couple of weeks and see, and if [your mood] doesn’t [improve],
then do it.” [...] So that’s what I did – I waited a couple of weeks, and it still was not
improving, and so I did increase it. – Jane, second trimester, taking antidepressants

Pregnant participants who deferred the decision about resuming antidepressants had stopped
taking antidepressants during pregnancy due to their desire to avoid harm to their baby.

It’s not really a risk that I feel like I wanna take without, you know... if I get severely
depressed or something, or my anxiety gets so bad to the point where every time I have
an anxiety attack I actually end up blacking out... if it gets to that point again, I’m going
to have to do something about it. But until then, I don’t want to have to take that risk. [...] I
might start both of the medications towards the end of the pregnancy... because I’ve got
a higher risk for the post-partum [depression]. They said that I’ve got a high chance for
that and that maybe I could start it towards the end of my pregnancy, if not start it after
the baby is born. I’m going to try not to. But we’ll see how it goes. If I have to do it, then
I have to do it. – Madison, third trimester, not taking antidepressants

Importantly, the threshold of severity that women defined for ‘needing’ to take
antidepressants depended on how women defined a desirable outcome. It was quite common for
women who chose not to take antidepressants in pregnancy to define a very stringent threshold –
with extremely severe symptoms of mental illness – at which antidepressants would be
necessary. Even if antidepressants might be needed for them to feel optimally mentally healthy,
they didn’t judge this outcome as important enough to override their desire not to take
antidepressants in pregnancy.

If my relationships are falling apart, and I’m feeling extremely unstable... if it’s affecting
my other kids and my family, then that’s something that you need to really think about.
Obviously, mine has not been to the point where I need to be hospitalized or I’m going to
be suicidal. If my degrees of decision-making are a little bit less... but I also don’t want to
be angry and depressed my whole pregnancy, which can also have ill-effects on the baby, so it’s kind of a gamble. – Rachel, third trimester, not taking antidepressants

One participant, Wakana, was unsure about how to judge when her symptoms had become severe ‘enough’ that she would ‘need’ to take antidepressants.

I don’t know how I would know? How bad do I have to be to take it? Hopefully I don’t need it. I have an appointment with [my reproductive psychiatrist] in early August... maybe I can wait until that day to talk to her about it. [My OB] said to expect to feel down for a few days after delivery, but if it lasts longer than 2 weeks, then this is depression, and maybe needs the medication. I forget what [my reproductive psychiatrist] said. – Wakana, third trimester, not taking antidepressants

Conflict-resolution strategies: Negotiating

Negotiating was another strategy that was used by most participants in response to discrepancies within their own beliefs/preferences or with those of their provider/partner/family. Negotiating was used not only to resolve the conflict, but also to lower women’s anxiety and to cultivate acceptance – or even conviction – in her own decision. For some women, who were attempting to resolve conflict with their provider/partner/family, these benefits of negotiation – lower anxiety and greater acceptance of the decision – were targeted towards their provider/partner/family, and were a main goal of negotiation.

The majority of participants encountered a conflict within their own beliefs/preferences; namely, between their medication necessity belief and their belief that taking antidepressants during pregnancy could cause harm to a baby. Many participants experienced a conflict between their own beliefs/preferences and those of their provider/partner/family. Many of these participants responded to these conflicts with negotiating tactics: conducting a physical experiment, and/or making a counter-offer.
Physical experiments as a negotiation tactic

Most participants who conducted a physical experiment in preconception or during pregnancy were attempting to reach a compromise – to make adjustments to be ‘safer’ or to demonstrate (to themselves or others) that they did everything they could to act in the best interests of their baby. In this context, physical experiments were focused on lowering risk of harm to a baby, and were associated with an increased risk of harm to the women themselves (consistent with female gender norms of self-sacrifice in caregiving). Results of these physical experiments informed decisions regarding whether it would be feasible to: 1) lower their antidepressant dose during pregnancy; or 2) to switch antidepressants to ‘safer’ ones for pregnancy.

Some participants were motivated to lower the dose of their antidepressant for pregnancy due to another medication belief – that the lower the dose, the lower the risk of harm to a baby. Thus, some women identified a goal to lower the dose of their antidepressants for pregnancy to the ‘lowest possible dose’ that they could take. For some of these women, the physical experiments revealed that they were already taking the lowest possible dose for them.

We did decide together - the psychiatrist and I - that I would try to get to the lowest effective dose for me... and so I started to do a taper, maybe a year ago, not with the intent of going off it, but with the intent of seeing, you know, from a teratogenicity standpoint, what was the lowest [dose] we could get to, and like the first drop probably, I ended up calling my primary [care provider] and asking like, “Is this withdrawal and it will pass?” And he’s like, “No, this is symptoms of the disease that we are treating, and this is why you need medication.” I’m like, “Okay. Alright then.” [Laughs] [...] I’m very happy to be on medication for life. I still would prefer if I could be mentally well for pregnancy and breastfeeding without medication because of the risks to baby so there is some amount of disappointment, but there was also a strong feeling of validation, a feeling of like, “No, no, no. I really need this. This is really right.” – Twyla, first trimester, taking antidepressants
A few participants contemplated trying to switch their antidepressants to a ‘safer’ option for pregnancy, but almost all eliminated this possibility quite quickly on the basis that this sort of change would be an ordeal.

I went through just a general search on depression and pregnancy, looking at just depression and pregnancy in general without treatment, and then looking at the effects of the different treatments, what medications have higher teratogenicity / side effects... did I want to have to go through transferring medication if I found some that was lower risk? That was quickly ruled out by my own self because I was like, "That could take years, let's not go there". - Carolyn, third trimester, taking antidepressants

Only one participant, Samantha, went ahead with trying to switch her antidepressant to a ‘safer’ option, and her expectations that it would be challenging were confirmed.

I’ve had some issues in this last little while. We were trying to switch me from the amitriptyline off to something because they were worried about anomalies with the amitriptyline and I literally went through four before I landed on Seroquel. [...] It’s quite a commitment to mix up your meds like this. [...] We had many talks about this, like do I want to mess with this? So yeah, it was a ton of conversations and definitely something that caused a lot of back and forth, and a lot of discussion and anxiety, for sure. Not an easy thing to think about rocking the boat on. – Samantha, preconception, planning to take antidepressants

Some participants categorized their decision to conduct a physical experiment as preliminary in order to manage anxiety associated with the increased risk to their mental health (associated with lowering their antidepressant dose, for example). Embedding flexibility into their mental health management plans offered women a way ‘out’ if the steps they took to protect their baby’s health ended up being too detrimental to their own health.

It was a little scary [to lower the dose of my medications], because since last summer it’s been so bad, I wasn’t sure what it would be like without that support. If I’d been dealing with my regular stuff, then I’d be okay, you know? But there’s been so much packed in on top of that, that I was nervous. What would it look like when I actually got down? But I also knew that there were other medications recommended, and I could try something a little bit different than what I was taking based on the data that was available... that there were more fairly safe medications, all things considered. – Hazel, third trimester, taking antidepressants
Some participants were not only categorizing their decision as preliminary for their own benefit and anxiety management, but also that of their health care provider/partner/family. For example, when Rebecca wanted to decrease the dose of her antidepressant in the third trimester of her pregnancy to lower the risk of her baby experiencing neonatal abstinence syndrome, both Rebecca’s partner and her providers were opposed to the plan – they wanted her to maintain the dose she was taking. In response, she categorized the decision as preliminary, to make it more palatable.

Because I was in such a strong position, mental health-wise, around week 30, I wanted to give it a try, of halving the dose. […] When I had this conversation with the Reproductive Mental Health psychiatrist and with my primary prenatal doctor, [what I said] was, “I'm very okay with going back to the 40[mg]. If it doesn't work, it doesn't work, and that's fine.”, because they were both quite concerned, which is fine, but I'm not going to, unlike other health decisions, where I'll tough it out for as long as I possibly can until there's a breaking point, I'm not going to do that in this circumstance. I think that the stakes are too high, in terms of there's already so much, with being a new parent, that we'll not add any more stress, and so there's no reason to suffer unnecessarily, and if I end up back on the 40[mg] tomorrow or next week, then that's fine. It's not a big deal. I don't feel like a failure. I will be glad that I tried [to decrease the dose] and then if it does work, and baby goes through less withdrawal, even better win. – Rebecca, third trimester, taking antidepressants

Making a counter-offer as a negotiation tactic

A few participants who did not want to take antidepressants, or who wanted to keep their dose as low as possible, made a counter-offer of committing to non-pharmacological treatment strategies, or a compromise of a very small dose change, when providers were suggesting the use of antidepressants or an increase in antidepressant dose (often in quite a paternalistic manner). For example, Elizabeth and Stephanie were committed to managing their mental health during pregnancy without antidepressants, and were willing to accept any recommendations or referrals for non-pharmacological treatment options, at least partially in the interests of appeasing their
health care providers and convincing them that it would be feasible to manage their mental health without antidepressants.

I told her I do not want to go on drugs, like ever, ever again. And she was like, “Okay, why?” And I told her, and she said, “Well, I understand, but if it comes to the point where you have severe postpartum depression and you're not bonding with your baby, I'm going to put my foot down”, and I said, “Okay that's fair”. I'm doing everything I can to avoid that, which is why I'm seeing the psychiatrist. – Stephanie, third trimester, not taking antidepressants

Synthesizing information: Assigning weight to information

It does throw the third variable in there, so you're no longer just thinking about side effects to yourself, you're looking at long term effect, both on and off the medication, so then you start looking at, okay, well if I'm not on it, then there's risks of low birth weight, and all the other stuff, but if I'm on... and my own health... and being able to take care of the baby, and so you start to get a bigger, more complex, flowchart or spreadsheet in your head of all these other things that you need to start weighing. – Carolyn, third trimester, taking antidepressants

Participants assigned weight to information on the basis of its topic (harm to baby or harm to self) and/or its type (expert opinion, stories of other women’s experiences, or scientific evidence and numbers). Participants’ beliefs and values – especially the medication necessity belief – underpinned this process. For the majority of participants, their initial instinct was to avoid risking any harm to their baby related to taking antidepressants in pregnancy. Most participants prioritized information from an expert over other types of information. Following information acquisition and synthesis, it was their medication necessity belief, in combination with their evaluation of the risk(s) of harm to their baby, that were pivotal in determining whether they chose to take antidepressants in pregnancy. If participants had no medication necessity belief, they typically engaged minimally in considering any other evidence; their decision not to take antidepressants was made on the basis that they weren’t needed.
Prioritizing risk of harm to a baby over risk of harm to themselves

In the vast majority of cases, participants’ default position was to prioritize a risk of harm to their baby as more important than a risk of harm to themselves (related to societal expectations of women and female gender norms - page 68). When participants encountered information that untreated depression during pregnancy could also cause harm to a baby (page 104), this simplified the decision for some women, but complicated it for others. This information made the decision simpler for women who either had strong medication necessity beliefs, or who were currently depressed during pregnancy, and who judged the likelihood of harm to their baby from antidepressants in pregnancy as low and/or minor in terms of severity. This reframing in their DM - to incorporate the information that pregnancy without antidepressants was also associated with risks - enabled participants to honor their desires to avoid causing harm to both their baby and themselves. This helped these women to solidify a decision to take antidepressants in pregnancy, and was an essential aspect of DM for most of the women who made this choice.

I had done enough reading to know that it’s not that maternal depression and anxiety are risk-free right? So, I didn’t feel like I was comparing a stratagem versus a natural pregnancy. I felt like I was comparing one intrinsic stratagem versus an extrinsic stratagem. – Twyla, first trimester, taking antidepressants

On the other hand, this information further complicated the decision for participants who had strong medication necessity beliefs, or who were currently depressed during pregnancy, but who weren’t convinced that the likelihood of harm to a baby from antidepressants in pregnancy was low and/or minor in terms of severity. In this case, women experienced high decisional conflict, which was particularly difficult for those who expressed a high level of stigma regarding their mental illness.

I’ve mostly resigned myself to needing [antidepressants] to function... but now, with considering pregnancy, I do feel like what’s wrong with me that I need these, and need to risk harming a little fetus ... baby ... and that I am putting my partner’s baby at risk (a bit
tearful). If there was another way... like I said, I’d suffer through it... but now that I know that depression during pregnancy is harmful to the baby... I guess if I thought there was a chance that I could not take antidepressants and not get depressed... but I just know that I need Wellbutrin to function... those years, when I wasn’t on it... I wasn’t functioning... – Olivia, preconception, undecided

The majority of participants who chose not to take antidepressants during pregnancy did not appear to have any knowledge of potential risks of harm to a baby due to untreated depression during pregnancy. There were only two participants, Rachel and Lena, who either chose not to take antidepressants during pregnancy (Rachel) or were leaning towards this decision (Lena), who mentioned an awareness of the potential risks of harm to a baby due to untreated depression during pregnancy. Participants, including Rachel and Lena, who chose not to take antidepressants during pregnancy either didn’t believe that they needed antidepressants (weak medication necessity belief) and/or prioritized the risk of harm to their baby as a result of antidepressants during pregnancy as more important than any risk of harm to themselves.

There were a few participants whose default position explicitly prioritized their health and identified a risk of harm to themselves as being of paramount importance. These participants chose to take antidepressants during pregnancy.

The fact that I was on Prozac was discussed quite forthrightly in my first prenatal appointment, and I was very okay with the idea... to prioritize my own health needs, which is actually healthier for the baby, but that's almost not the point. It was a decision that, actually, wasn't made for the best interests of the child, it was made in the best interests of me. I refuse to buy into the notion that I need to be a complete martyr for this baby. I'm just not going to do that, and the reason for that is, I think, a strong confidence in this feminist identity. Those narratives are awful, of mothering and how you're supposed to completely give yourself over as a vessel, and so I actually see it as a political act to not do that and to not feel guilty about it. Yeah, it was definitely more of a big picture decision... this aligns with my values as a woman, as a feminist, as a human, as a human with health needs. Yeah, it was definitely a very deliberate political act. – Rebecca, third trimester, taking antidepressants
Expert opinion, stories, or scientific evidence/numbers?

The majority of participants assigned the most weight to expert opinion in their DM, with many expressing that it was the single more important factor in their decision.

What was the most influential? I think the doctor I saw [at BC Women’s Hospital], [the reproductive psychiatrist] . . . I think the reassurance from her, like she seemed so confident. She was just so confident and reassuring. I felt very comfortable right from that day. And I trusted her. I feel like I trust this hospital [BCWH]? I feel like there’s a good reputation with people that work here and I just – yeah, that was really it that made me the most comfortable. – Stacy, third trimester, taking antidepressants

Participants prioritized expert opinion for different reasons. Some participants identified the ‘real life’ experience of experts as being the most valuable, and explicitly assigned more weight to information from experts due to their experiences of caring for other women, as opposed to their access to the latest evidence, for example.

It was very reassuring, having a resource like Motherisk and then also talking to my midwives, who have dealt with people who have been on medication and been fine, and then talking to [my reproductive psychiatrist] … so I think, for me, having real people with real experience, versus going online and seeing this study, and 2 and 3% and that sort of thing, that was harder for me to grasp, whereas, coming from people with experience, it was a lot more reassuring. – Sarah, second trimester, taking antidepressants

On the other hand, a few participants articulated that they assigned more weight to information from experts because they appreciated the expert’s knowledge and interpretation of available scientific evidence.

I don’t try to manage my own health care; I believe that’s what the doctors are for... I just want to know what I’m dealing with most of the time, and then let the people that spend their lives learning about this stuff do what they do. [...] I did have discussions with the psychiatrist, prior to actively trying [to conceive], about the risks and benefits of antidepressants with pregnancy... it was like, “Ok, just give me the facts and let’s figure it out”. – Gail, third trimester, taking antidepressants

A few participants assigned the most weight in their DM to stories that they heard directly from other women (not indirectly through an expert’s experience). From Whitney’s
perspective, for example, the experience of a friend was significantly more influential than the advice of a physician in her decision to take antidepressants.

I would definitely say talking to [my friend] who’d gone through it, and who’d done that [taken antidepressants in pregnancy], and seen the changes, and not had a lot of adverse effects was . . . And someone who I trusted, you know? ... definitely way more than anything I read. And definitely way more than having the psychiatrist say, “Here: I think you should take this”, right? You know, if you’re a little bit unsure about it, you’re never going to listen to the doctor. – Whitney, third trimester, taking antidepressants

As Lena elaborated, part of the value of hearing the stories of other women, either indirectly from experts or directly from other women, is the transformation of the abstract (i.e., aggregate data and statistics) into the concrete (i.e., what the experience would actually be like).

I would say that my friend's story of a successful pregnancy on antidepressants was a much stronger piece of information than looking at the papers, and looking at the x-percentage of this and that. I think we all want to make decisions that way, but it's pretty hard with those types of information. I think when I was reading some of the academic papers on it, it's really hard for me to grapple with what the actual consequences are of some of these side effects. For example, when I spoke to the [reproductive psychiatrist], she had mentioned some babies experience a little withdrawal from the antidepressant, which is really she'll get a fussiness, like feeding and stuff. And then you read about it in this paper, and it sounds way worse than what she had described it as. So, yeah, there is a bit of that disconnect between, I guess, statistical significance and clinical significance... what it actually means. So, it's hard to read those papers and really grasp what they mean.  
– Lena, preconception, undecided

**The role of sharing decision making**

The majority of participants worked through the DM activity clusters and synthesizing processes, at least partially, with a health care provider or partner (or both). Most found sharing the DM helped them in reaching a decision, and many participants expressed gratitude for the DM support that they received. In particular, when participants were having difficulty reaching a decision, choosing to share the DM with someone else was often the catalyst that enabled them to reach a decision. However, most still felt that they shouldered the primary responsibility for
deciding how to manage their mental health in pregnancy. A few women preferred to maintain control over the DM process, and chose to undertake the entirety of this work.

Making the decision with a health care provider

For many participants, consulting with a health care provider was a key step in reaching a decision. This was particularly true for providers that they trusted and/or saw as an expert (page 91), and was the case for participants who chose to take antidepressants and who chose not to take antidepressants (page 121). It was especially helpful when the provider engaged with them in not only providing information, but also in making sense of the information and supporting them in managing their emotions. Unfortunately, women who desired such DM support did not universally receive it from the health care providers with whom they consulted (page 64). A few participants reported disappointment in paternalistic interactions with providers who offered only their opinion, rather than supporting them to reach their own decision, and/or that providers shared only information, without corresponding support.

So, I went and saw the psychiatrist who specializes in women’s health and had a horrible experience. I don’t know if it’s just her, and her bedside manner, or if I set us up for failure by priming her that I’m a [health care provider] and that I’m someone who really wants to know data, but I felt like I didn’t get any sort of synthesis or big picture, and definitely not any decision-making support. And she left me this awful voicemail afterwards where she’s like, “Oh I forgot to review these couple of studies with you...” and leaves on this voicemail this data... It was like some publications linking it to autism or something, and I’m like, “Really? Really?” [...] I didn’t feel like, even from a just educational, medical standpoint, like counselling aside, I didn’t feel like she helped me make sense of the data. I never felt like I got an overarching clinical opinion... not at all as a black or white, “Is this safe?”, but some sort of synthesis. – Twyla, first trimester, taking antidepressants

Making the decision with a romantic partner

For many participants, a romantic partner did not feature particularly prominently in their DM processes. Most of these women made the decision and then, if they had a partner, informed
their partner of the decision. They typically characterized their partner as being supportive of their decision and/or DM processes, and some mentioned the importance of retaining autonomy over decisions related to their body.

“I spoke to my husband. And he is supportive in whatever I want to do and feels right, he’ll support me in my decision.” – Elizabeth, second trimester, not taking antidepressants

On the other hand, participants were usually keenly aware that they were making decisions on behalf of their partner’s baby, and were often concerned about the potential impact on their relationship with the co-parent if their decision caused harm to the baby.

When we were talking to the psychiatrist, [my partner said]: "I don’t. I would never blame you or anything", but I feel like he does though. I feel like he would blame me; I would blame me. He gets pissed off about like... I don’t want our kids’ mom to be like, “Oh sorry, I have lung cancer because I was an idiot when I was young.” He gets really mad about me smoking and stuff... unhealthy behaviours he’s not keen on. So I feel like he would be upset, yeah. I feel like anybody... and he’s a wonderful man, but I feel like any man would be like... even the best of them would be like, “This is your fault.” – Desiree, preconception, undecided

Some participants did involve their partner in their mental health treatment decision more actively. In these cases, women found that this enabled them to reach a decision.

Once I read the [psychiatrist’s letter summarizing our appointment], I was like, okay... because in the psychiatrist report, she’d actually referred to some of the statistics, and stuff, and I’m, okay, I’m going to bring my husband into this, because this is our baby together, and so I read it to him, and then we went on the Motherisk website, and we looked at the different studies, and he was like – he’s a very practical engineer, all about numbers - and so he was very much like, “No, I agree with your decision. I support your decision to stay on it. I think that’s wise.” So that’s what I did. [...] if my husband, as the father of the child... if you have a baby with some kind of defect, it’s his baby too, and I don’t want to be the sole decision maker in that. – Jane, second trimester, taking antidepressants

**Trying to live with the decision**

Some participants had difficulty accepting their decision and letting it go; they continued to return to the DM process to ruminate over the options and engage in thought experiments
(page 100). For these participants, repeating a mantra was insufficient (page 111). They had a history of anxiety as well as depression, and had either decided to take antidepressants during pregnancy, or were still undecided. These women devoted a lot of energy as part of preconception planning to deciding how to manage their mental health during pregnancy, and it was usually prior to pregnancy that they identified their difficulty in letting go of the DM process to settle on a decision. Those that had made a decision at the time of the interview had realized that they needed to explicitly recognize for themselves that they had confidence in their decision and were choosing to let it go.

After going through and wrestling - because I really, really was, you know, and sometimes I still do - I think I need to have like, “okay, this is where I’m going to be, I’m going to just live with this decision.” – *Samantha, preconception, planning to take antidepressants*

In addition to making the conscious choice to accept their decision, these participants used some other tactics in their process of settling on a decision. These included: acknowledging the limits of what can be controlled, and showing themselves that they had behaved responsibly. When women acknowledged the limits of what can be controlled in this context, they reflected on how choosing to have a child always involves risk and that – even if they have a child with some sort of developmental anomaly – it may not be attributable to their prenatal antidepressant use.

I went into pregnancy saying to myself, “This can go two ways. You can either feed the anxiety, and add worry about every single thing you eat, and every pill you take...” And knowing I’m an anxiety-prone person, I knew that if I started down that road, it would not be good. So, I went into it, with my husband’s support and everything, as “I’m going to be as relaxed as possible about medication use”, because otherwise it’s just going to be this big ball of guilt, and like what if... what if... what if...? I had to consciously shut that down and say, “You’ve made your decision. If something terrible happens, and there’s a defect, yes, that would be terrible”... however, you couldn’t actually ever really say that it was the... like, heart defects are pretty common actually. So, you just have to make the decision, and then deal with whatever. – *Jane, second trimester, taking antidepressants*
Alternatively, women reassured themselves that they had behaved responsibly by reviewing the integrity of their DM process and all the preconception steps that they had taken to promote optimal outcomes for themselves and their family.

I think it was good that I started the decision-making process when I was in a good spot. A good spot mentally, where I can sit down and be very rational about it, and actually look at the facts, look at everything in an even playing field, and lay out all the facts for myself. So I think that helped, being in that good mental state and healthy mental place before getting pregnant, and before having to make all these other decisions. I was able to lay out the base and say, "Okay this is what I'm basing it on". [...] I was able to get referred to the [Reproductive Mental Health clinic] early on to have a consult about my concerns there. So, trying to be proactive with it, rather than just letting it happen. It's like, “No, no, I need to know this, to feel comfortable with the decision and the risks that could happen.” – Carolyn, third trimester, taking antidepressants

As part of recognizing their own responsible behaviour, women sometimes invoked the language of having done their “due diligence”.

I have made this decision feeling like I've done quite a bit of due diligence. [...] I got the information that I need to make this decision, and now I can do it confidently.” – Lena, preconception, undecided

Participant feedback: Follow-up interviews

Overall, participant reactions to the model and results summary were positive. Participants agreed that results generally fit with their experience and that there was nothing major that was missing. Some participants shared suggestions for minor changes to the model, and wanted to discuss plans for sharing the results with a broader audience (Table 2.3).
Table 2.3. Participant feedback

<table>
<thead>
<tr>
<th>Participant</th>
<th>Decision at first interview</th>
<th>Positive feedback</th>
<th>Suggestions for change</th>
<th>Researcher response to suggestions for change</th>
<th>Comments on model utility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Twyla</td>
<td>Taking antidepressants</td>
<td>Really liked two particular things: 1) model was very process-oriented and dynamic, 2) that it was very contextualized</td>
<td>Consider explicitly including partner or family as a contextual factor in the model</td>
<td>From the study data, partner/family exerted influence at the level of information processing – seen particularly in the ‘making sense of information’ cluster – rather than at the higher level of contextual factors</td>
<td>Didn’t ask and wasn’t volunteered</td>
</tr>
<tr>
<td>Nadia</td>
<td>Taking antidepressants</td>
<td>“It reflected my experience for sure.” The diagram was a nice way of laying it all out – multi-layered, all the different influences on the DM process</td>
<td>None</td>
<td>N/A</td>
<td>“I didn’t really get information presented to me that I was part of a larger group of women making these decisions until much later in my journey. It would be helpful for clinicians – not just RMH, but primary care clinicians. By the time I got in touch with the RMH group, they are obviously very aware and more sensitive to the DM process and choosing your best options, but not at the primary level for sure – that’s where I thought it would be very useful.”</td>
</tr>
</tbody>
</table>

Notes. Acronyms used in quotes in the interests of space. DM = decision making RMH = the Reproductive Mental Health program
<table>
<thead>
<tr>
<th>Participant</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Natsumi</td>
<td>Not taking antidepressants</td>
<td>“It’s a very flowy representation... it’s not like a linear thing. You can go in and out of all these circles and levels and clusters of thoughts.” “I really liked the terms self-soothing, gatekeeping... really liked ‘is this info trustworthy?’ – that was a good one too.” “The self-soothing I really liked. That’s a thing that really happens! Like, you have to get some type of defense or some type of thing to make yourself feel better. I liked that that was identified that after all the information, you need something to help you deal with that.”</td>
<td>“The only thing that I thought about was the aspect of time, but then it is represented by the like first trimester, second trimester... like the purple circle; like when you make a decision at a given point in time and mental space, you might make a certain decision, and then fast forward to a different time-moment and space, you might make a completely different decision; so yeah, I feel like that is represented by your model, but I guess I just had to think about it for a little bit.... something about the aspect of time... but then you can totally tell that that is “time” because it’s like the different phases of pregnancy... I was talking to a friend about how certain decisions in pregnancy are so “in the moment”... that desperation aspect – that bubble of time, that pressure... being so either depressed or something... like maybe you’d choose something that you wouldn’t have otherwise chosen if you weren’t in that pressurized bubble... but I don’t know what that is... I guess ‘mental state’ maybe?”</td>
<td>This feedback inspired me to consider further how I was representing and discussing contextual factors in the DM environment. As a result, I created a new subsection in ‘contextual factors’ (page 60) that more clearly communicated the three layers of the emotional/cognitive environments that influenced participants’ DM.</td>
<td>Interested in collaborating on future knowledge translation efforts.</td>
</tr>
</tbody>
</table>

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</tr>
</thead>
<tbody>
<tr>
<td>Rachel</td>
<td>Not taking antidepressants</td>
<td>“It was pretty accurate. It was basically everything that I said.”</td>
<td>None</td>
<td>N/A</td>
<td>Didn’t ask and wasn’t volunteered</td>
</tr>
<tr>
<td>Najdah</td>
<td>Undecided</td>
<td>“It’s nice to see it all in a diagram like that. I like it a lot.”</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>“It’s nice to see it because there are certain things that I wasn’t even aware of that are true to me as well... like patriarchy, I never looked at it that way, but yeah – it’s totally true.”</td>
<td>None</td>
<td>N/A</td>
<td>“It’s so nice to see it like this. It helps you structure your own journey... provide a little bit of a structure to what you’ve been through and all that. ‘Coz right now I’m just putting my experience into the different buckets... this is where I was anxious, this is where I was guilty...’”</td>
</tr>
</tbody>
</table>

**Notes.** Acronyms used in quotes in the interests of space. DM = decision making RMH = the Reproductive Mental Health program
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</tr>
</thead>
<tbody>
<tr>
<td>Sofia</td>
<td>Undecided</td>
<td>“[the components in the model] identify on the outside what I feel like my experience has been.” “I haven’t experienced pregnancy yet with medication or not, but just in general when you’re experiencing mental health, you do go through all those processes with decisions, right?” “the results, it’s like pretty... I mean, maybe it’s because I’ve been there, that like they’re pretty – visually explain pretty much what goes on. I don’t know how somebody who has not experienced depression or had to deal with this decision would read it in the same way that I do?”</td>
<td>Could articulate more explicitly that the “decision” in the model can include deciding to defer the decision regarding taking antidepressants in pregnancy. “it’s kind of silly, but it's like, we don’t even know the options of the decisions we can make... or that, you know, it’s a decision...” Sofia also reflected that there are so many other decisions that can be wrapped up in the decision regarding antidepressant use in pregnancy. “If I were to get pregnant [now] like kind of by chance, my decision would be in like the 1st trimester period, and would be like: “Do I continue this pregnancy or do I end it?”</td>
<td>I kept this feedback in mind while revising the section “Reaching a decision ... or not” (page 118), and have highlighted this dimension of the model in the subsection dedicated to deferring the decision (page 126).</td>
<td>“Definitely for patients... this would be part of maybe the normalization ‘coz, like, if somebody looks at it and sees – ok, there’s been this study, then immediately, you know, ok, there’s other people like me... and when you see that, you see yourself represented and you know, others have felt similar to what I’m feeling...” “I don’t know how the physicians would take it, but definitely into more like an educational, like, listen, this is what women who are dealing with depression during their reproductive age, like – this is a gap, and this is what is going on in their world... like, this is how they are approaching the decision.”</td>
</tr>
</tbody>
</table>

*Notes. Acronyms used in quotes in the interests of space. DM = decision making RMH = the Reproductive Mental Health program*
Discussion

This constructivist, woman-centred, grounded theoretical model of women’s DM regarding mental health care in pregnancy builds on previous work to offer a deeper, more complex portrayal of this experience. The multi-layered, dynamic, and iterative structure of our theory intends to honor the complexity and relationality of women’s lives, in keeping with my feminist theoretical framework.

Our theory has much in common with the only other theory that has been published on this topic, Nygaard’s constructivist grounded theory (which used ‘modified’ methodology \( N=8 \))\(^{110}\), but our extension of that work adds depth and nuance to published understandings of this DM process. The core category of Balancing Risk identified in Nygaard’s theory is visible in our model, embedded within the Seeking Information and Making Sense of Information clusters of DM activities, and also in the overarching process to synthesize information towards reaching a decision, Assigning Weight to Information. Nygaard’s model’s subcategory of Assessing Depression and Antidepressants highlights the importance of: the participants’ medication necessity and illness beliefs; the connection participants made between prenatal antidepressant use and “the moral responsibility of being a mother”\(^{110}(p. 488)\); receiving information from a specialist about the risk of untreated depression; perceptions of infant health outcomes as being possibly unrelated to prenatal antidepressant use; and their previous experiences with depression and its treatment. These themes are also included in our model in: Contextual Factors – Patriarchy; Seeking Information; Making Sense of Information; Synthesizing Information – Assigning Weight to Information; and Reaching a Decision... or Not – Trying to Live with the Decision. Nygaard’s model’s subcategory of Evaluating the Impact of Significant Others
emphasizes the role of: social support; sharing DM with partners and care providers; self-protection by only discussing their decision regarding antidepressants with trusted others; conflicts between beliefs and preferences of significant others; creating a “psychosocial safety net”\textsuperscript{110}(p. 489); and framing their decision as the “right” decision of a “good mother”\textsuperscript{110}(p. 490). These themes can be found in our model in: Self-soothing; and Reaching a Decision ... or Not. In an extension to Nygaard’s model, consistent with my feminist theoretical framework, we privileged women’s emotional and societal context in our DM theory.

Specifically, our “self-soothing” cluster of decision-making activities represents a unique contribution to the literature. While some previous studies reported that women experienced strong negative emotions of anxiety\textsuperscript{112}, guilt\textsuperscript{111}, and fear\textsuperscript{111} in their decision-making process, they did not comment on how women responded to these emotions, or the role of emotions in their decision making. The presentation of findings by Nygaard (2015) did not label emotions at all, although an important part of their core category of Balancing Risk was how women dealt with risk and uncertainty, including their efforts to create narratives for themselves that justified their choice as that of a “good mother”. Our explicit labelling in our decision-making theory of emotions, and women’s responses to those emotions, privileges this aspect of women’s lived experiences, which not only does justice to the women’s stories, but is also appropriate to my feminist framework. Emotions played a central role in women’s decision making, and are thus close to women in the visual depiction of the model, and the self-soothing cluster of activities is the same size as the seeking information and making sense of information clusters of activities, highlighting that it is of equal importance in the decision-making process.

Our model shares feminist underpinnings with the Wittmann-Price TEDMWH\textsuperscript{83}, which has been used in an exploration of satisfaction with DM regarding medication use for depression
and/or anxiety during pregnancy. In the Wittmann-Price TEDMWH, there are three components of emancipated DM: personal knowledge, awareness of social norms, and a flexible environment. In this theory, personal knowledge involves self-awareness – in terms of emotions and the potential impact of decision options on the decision maker’s life. Awareness of social norms acknowledges that societal standards have designated one decisional choice as preferable compared to others. A flexible environment emphasizes the importance of a non-judgmental space in which women are free to choose any of the available options. Our theory is philosophically congruent and thematically consistent with the Wittmann-Price TEDMWH, however, it focuses more on operationalizing the processes followed by women in DM. In doing so, our theory densifies and connects women’s DM processes, proposing a structure by which DM occurs. It is, thus, more process-focused than outcomes-focused.

The broader literature examining women’s perspectives of treatment decision making during pregnancy is fairly limited, however, we can compare our findings to those from studies of women’s decision making for use during pregnancy of the following types of treatment: antipsychotic or mood stabilizing medication, anti-nausea medication, gastric and antibiotic medications, and pertussis vaccination. The strongest, consistent message across these studies is women’s desire to protect their babies, and the prioritization of their baby’s health in the decision-making process (often at significant cost to themselves). Societal expectations of “good motherhood” appear to be pervasive in decision-making processes, regardless of the type of treatment under consideration.

It is unsurprising that “good motherhood” features prominently in women’s decision making during pregnancy considering the overwhelming variety of topics about which (prospective) mothers are given advice, in the context of a patriarchal society that defines women’s identity in
terms of caregiving\textsuperscript{167–170}. Current parenting culture sets high standards for mothers and emphasizes self-sacrifice\textsuperscript{171–173}, which can lead women to fear censure of their behaviour and feel pressure to construct a narrative that justifies their behaviour as being morally responsible\textsuperscript{170,174}.

While women across illness and treatment contexts strive to fulfill their roles as “good mothers”, this goal seems to be foregrounded to a greater extent in the decision-making of mothers with a history of psychiatric illness, who are making decisions about psychiatric medications. Interestingly, the narratives around “good motherhood” as a justification for decisions about antidepressant use also appear in the only two studies that report women’s experiences of decision making for antidepressants outside the context of pregnancy\textsuperscript{99,100}. A potential explanation for this could relate to the intersection of the stigma of mental illness and female gender norms, with these mothers feeling a greater need to justify that their behaviour is conforming to societal norms.

A further difference between women’s decision making about psychiatric medications, compared to other pharmaceuticals, is their treatment-associated risk perceptions. In a study in which women called the Motherisk helpline for information about the risks associated with taking antidepressants, gastric medication, or antibiotics during pregnancy, a substantially greater proportion of women (87%) estimated that the risk of antidepressants was higher than 1-3%, compared to that for gastric medications (56%), or antibiotics (22%) [the actual risk of all three groups of medications was estimated by the authors as 1-3%]\textsuperscript{118}. Further, women calling about antidepressants were less likely to revise their initial assessment following the provision of this evidence, with 12% of women estimating the risk of antidepressants as higher than 1-3% post-counselling, compared to 4% of women calling about gastric medications and 2% about
antibiotics. This also correlated with women being more likely to discontinue their antidepressants compared to women in the other study groups.

In addition to potentially greater internal pressure within women to discontinue psychotropic medication during pregnancy (as compared to treatment for other indications), the role of pressure from health care providers to discontinue psychotropic medication during pregnancy – as seen in the ‘patriarchy in health care’ element of our theory – is quite striking. While some elements of patriarchy in health care were evident in the studies reporting women’s experiences of decision making for anti-nausea medications and pertussis vaccination – namely, women felt that they hadn’t received sufficient information from providers – the experiences of women being encouraged to forego, or worse, denied access to, medication that is vital for their health is potentially unique to psychiatric medication use in pregnancy.

**Limitations**

This study focused only on the experiences of pregnant and preconception women; the experiences of health care providers supporting women in their DM and also the experiences of significant others, for example, the romantic partners of pregnant women, would provide insight into other dimensions of the DM process. However, the prioritization of the women’s perspectives aligns with the feminist theoretical framework which provided a foundation for the work.

It is important to note that all participants had access to stable housing, were connected with the healthcare system to at least some extent, and all those with a reported history of addictions were in recovery. The DM process for mental health care in the perinatal period could be different for women who are homeless, who are disconnected from health care providers, and/or who have active addictions. There could also be differences in the DM process for women
of different cultural groups. We did include an interview question designed to explore a potential influence of cultural background on participants’ DM, and CH was sensitized to concepts of intersectional identities during the interviews. Participants did not generally highlight an impact of any cultural groups with which they identified on their DM, and so this was not pursued aggressively in theoretical sampling.

These limitations would be a threat to generalizability for research conducted using a (post)positivist paradigm, however, they are much less concerning for this research given that the constructivist paradigm embraces the situational and co-constructed nature of knowledge and does not seek to uncover an objective reality that applies to all women.

We did not collect data regarding participants’ current mood symptoms, however, based on participants’ self-report and CH’s extensive experience with clinical research interviewing with this population, it seemed that participants who chose not to take antidepressants during pregnancy experienced more symptoms of depression than those who chose to take antidepressants during pregnancy. Current symptoms of depression were evident in the interview data with longer response latency, slower pace of response, and less detailed replies. The lower quality of data from interviews with women who were currently depressed could have biased the analysis in favour of the DM processes of women who were mentally well at the time of the interview. Further, CH’s personal experience of choosing to take antidepressants during pregnancy could have biased the analysis in favour of the DM processes of women who chose to take antidepressants during pregnancy. Reflexivity, peer debriefing, expert audit, and continual focus on disconfirmatory evidence were strategies used by the research team in an effort to re-balance the analysis to represent the voices of all the participants.
Chapter 3: Exploring a potential impact of variations in the pharmacogenes *CYP2D6* and *CYP2C19* on depression symptoms in the context of SSRI use during pregnancy.
Purpose

The purpose of this study was to test the hypothesis that women with deleterious variants in the pharmacogenes \textit{CYP2D6} or \textit{CYP2C19}, taking selective serotonin reuptake inhibitors (SSRIs) prenatally, would have more depression symptoms than women whose pharmacogenetic variants have been associated with normal SSRI metabolism.

Methods

Data collection

Participants were recruited as part of prospective, longitudinal cohort studies focussed on 1) evaluating risk factors for postpartum mental illness amongst high-risk women (Dr. Austin’s cohort; cohort A)\textsuperscript{175} and 2) impact of SSRI use or maternal mental illness during pregnancy on infant development and behaviour (Dr. Oberlander’s cohort, cohort O)\textsuperscript{176–178}. Cohort A was recruited between 2007 – 2016. Cohort O was comprised of two cohorts, with very similar procedures and characteristics – cohort O1 recruited between 2002 – 2005, cohort O2 from 2006 – 2010. Pregnant, English-speaking women were recruited from the Greater Vancouver area through community advertising or from the BC Reproductive Mental Health program. As part of extensive data collection including clinical interviews, questionnaires, and blood draws, participants completed the Edinburgh Postnatal Depression Scale (EPDS) to measure symptoms of depression (page 153), and provided details in terms of SSRI dose (if applicable), weight, and gestational age (self-reported). Studies were approved by the UBC/Children’s and Women’s Hospital ethics boards (cohort A: H06–70145; cohort O1: H00-70500; cohort O2: H05-70629).
From the two cohorts, there were 83 participants who were eligible for analysis. These were participants who were regularly taking paroxetine, sertraline, citalopram, or escitalopram at the time of enrollment, for whom DNA or pharmacogenomic analysis results were available, and for whom an EPDS score during pregnancy was available. Blood or extracted DNA samples from both cohorts were stored in -80°C freezers between collection and analysis.

**Measurement scale**

The Edinburgh Postnatal Depression Scale (EPDS; self-report, 10 Likert-type items; Appendix V)\(^\text{179}\) was designed for perinatal use to assess symptoms of depression, has strong reliability (\(\alpha=0.87\)) and is validated for prenatal use\(^\text{180}\), including in high-risk pregnancies\(^\text{181}\). It is the gold standard for both research and clinical use and has been extensively validated in many languages and cultural groups\(^\text{182–186}\). Higher EPDS scores indicate more depression symptoms (range: 0-30). An EPDS score of 15 or higher during pregnancy has a sensitivity of 100% and a positive predictive value of 60% for major depression (with a false-positive rate of 4\%\(^\text{180,187}\).

**Pharmacogenetic analyses**

DNA was extracted from blood samples, purified, and quantified according to published protocol\(^\text{188}\). Cohort O samples were analyzed by Dr. Gaedigk’s lab; Cohort A samples were analyzed by Dr. Ross’ lab. Cohort O1 were genotyped using restriction fragment length polymorphism (RFLP) assays carried out on a 6.6 kb long-range PCR (XL-PCR) fragment encompassing the \(CYP2D6\) gene. Cohort O2 were genotyped using commercially available TaqMan assays (Applied Biosystems, now Thermo Fischer Scientific, Waltham, MA) directly on gDNA. Eight \(\mu\)l reactions were performed in 96-well plates under the conditions recommended by the manufacturer. Cohort A were genotyped using a custom pharmacogenomic genotyping
panel consisting of pre-plated TaqMan assays (Applied Biosystems, now Thermo Fischer Scientific, Waltham, MA). Reactions (10 µl with 10 ng DNA per reaction) were performed in 384-well plates on the QuantStudio 7.0 Real Time PCR System (Thermo-Scientific). Alleles genotyped for each cohort are shown in Table 3.1.
Table 3.1. Genotyping summary

<table>
<thead>
<tr>
<th>Allele1</th>
<th>Genotyping approach used</th>
<th>rs ID2</th>
<th>Genetic variation (e.g., SNP)</th>
<th>Region targeted3</th>
<th>Participants tested</th>
<th>Cohort O1</th>
<th>Cohort O2</th>
<th>Cohort A</th>
</tr>
</thead>
<tbody>
<tr>
<td>*2, *17, *29, *41</td>
<td>RFLP or TaqMan</td>
<td>rs16947</td>
<td>C&gt;T</td>
<td>2850</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>*3</td>
<td>RFLP or TaqMan</td>
<td>rs35742686</td>
<td>A-del</td>
<td>2549</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
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<tr>
<td>*4</td>
<td>RFLP or TaqMan</td>
<td>rs3892097</td>
<td>G&gt;A</td>
<td>1846</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
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<tr>
<td>*6</td>
<td>RFLP or TaqMan</td>
<td>rs5030655</td>
<td>T-del</td>
<td>1707</td>
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<td>Yes</td>
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<tr>
<td>*7</td>
<td>RFLP or TaqMan</td>
<td>rs5030867</td>
<td>A&gt;C</td>
<td>2935</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td></td>
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<tr>
<td>*8, *14</td>
<td>RFLP</td>
<td>rs5030865</td>
<td>G&gt;T</td>
<td>1758</td>
<td>A subset</td>
<td>No</td>
<td>No</td>
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<tr>
<td>*9</td>
<td>TaqMan</td>
<td>rs5030656</td>
<td>AAG-del</td>
<td>2615</td>
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<td>No</td>
<td>Yes</td>
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<tr>
<td>*4, *10, *36</td>
<td>RFLP or TaqMan</td>
<td>rs1065852</td>
<td>C&gt;T</td>
<td>100</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

1 Some SNPs are part of multiple allele definitions (haplotypes) and may occur on alleles not shown here. The table lists only those alleles identified.

2 rs IDs are not available for some gene deletions, duplications, or conversions.

3 Position coordinates are for CYP2D6*1 reference sequence M33388, which has been used by the nomenclature committee. Allele definitions are as described by the Pharmacogene Variation Consortium at [www.PharmVar.org](http://www.PharmVar.org).
<table>
<thead>
<tr>
<th>Allele$^1$</th>
<th>Genotyping approach used</th>
<th>rs ID$^2$</th>
<th>Genetic variation (e.g., SNP)</th>
<th>Region targeted$^3$</th>
<th>Participants tested</th>
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<tbody>
<tr>
<td>*11</td>
<td>RFLP or TaqMan</td>
<td>rs201377835</td>
<td>G&gt;C</td>
<td>883</td>
<td>A subset$^4$</td>
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<td>*17</td>
<td>RFLP or TaqMan</td>
<td>rs28371706</td>
<td>C&gt;T</td>
<td>1023</td>
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<tr>
<td>*29</td>
<td>RFLP or TaqMan</td>
<td>rs59421388</td>
<td>G&gt;A</td>
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<tr>
<td>*41</td>
<td>RFLP or TaqMan</td>
<td>rs28371725</td>
<td>G&gt;A</td>
<td>2988</td>
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<td>*5</td>
<td>XL-PCR or TaqMan$^6$</td>
<td>N/A</td>
<td>Gene deletion</td>
<td></td>
<td>A subset</td>
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<tr>
<td>xN</td>
<td>XL-PCR or TaqMan$^7$</td>
<td>N/A</td>
<td>Gene duplication or multiplication</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>*36</td>
<td>RFLP or TaqMan</td>
<td>N/A</td>
<td>Exon 9 conversion</td>
<td></td>
<td>A subset</td>
</tr>
<tr>
<td>*13</td>
<td>XL-PCR or TaqMan</td>
<td>N/A</td>
<td>CYP2D7-2D6 hybrid genes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>*2</td>
<td>TaqMan</td>
<td>rs4244285</td>
<td>G&gt;A</td>
<td>c.681</td>
<td>Yes</td>
</tr>
<tr>
<td>*3</td>
<td>TaqMan</td>
<td>rs4986893</td>
<td>G&gt;A</td>
<td>c.636</td>
<td>Yes</td>
</tr>
<tr>
<td>*4</td>
<td>TaqMan</td>
<td>rs28399504</td>
<td>A&gt;G</td>
<td>c.1</td>
<td>Yes</td>
</tr>
<tr>
<td>*17</td>
<td>TaqMan</td>
<td>rs12248560</td>
<td>C&gt;T</td>
<td>g.-806</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CYP2C19</th>
</tr>
</thead>
<tbody>
<tr>
<td>*2</td>
</tr>
<tr>
<td>*3</td>
</tr>
<tr>
<td>*4</td>
</tr>
<tr>
<td>*17</td>
</tr>
</tbody>
</table>

$^1$ Some SNPs are part of multiple allele definitions (haplotypes) and may occur on alleles not shown here. The table lists only those alleles identified.

$^2$ rs IDs are not available for some gene deletions, duplications, or conversions.

$^3$ Position coordinates are for CYP2D6*1 reference sequence M33388, which has been used by the nomenclature committee. Allele definitions are as described by the Pharmacogene Variation Consortium at [www.PharmVar.org](http://www.PharmVar.org).

$^4$ For cohort O, participants positive for 2850T (variant), but negative for SNPs identifying *17, *29, or *41 were selected for testing for the presence of the rare *11 allele in cohorts O1 and O2, and the rare *8, and *14 alleles in cohort O1. Further, XL-PCR was performed on all cohort O samples to detect the presence of a gene duplication or multiplication (xN). All samples with an initial homozygous genotyping result were also tested by XL-PCR for the presence of the CYP2D6*5 gene deletion. Participants carrying the 100C>T SNP (i.e., were heterozygous C/T or
homozygous T/T) were selected for testing for the presence of the \textit{CYP2D7}-derived exon 9 conversion indicative of *36. For cohort O1, the presence of the exon 9 conversion was tested by RFLP analysis; for cohort O2, by a quantitative multiplex PCR method described elsewhere\textsuperscript{189}. All samples were tested by XL-PCR for the presence of Fragment B, which targets the intergenic region between duplicated gene copies. Fragment B is only amplified if a duplication event is present, and the additional gene copy has a \textit{CYP2D6}-derived downstream structure. For example, \textit{CYP2D6}\textsuperscript{*1xN}, \textit{*2xN}, \textit{*4xN} will amplify fragment B, while \textit{*36+*10} will not. All samples positive for Fragment B were selected for testing using Fragment D (an XL-PCR fragment encompassing the entire duplicated gene unit). Fragment D was amplified and subsequently genotyped to determine which allele was duplicated or multiplicated, to discriminate between \textit{CYP2D6}\textsuperscript{*1xN}, \textit{*2xN}, \textit{*4xN}, etc. This fragment is amplified regardless of whether the duplication event has a \textit{CYP2D6} or \textit{2D7}-derived downstream region.

The following were not genotyped for all cohorts due to their low population frequencies: \textit{CYP2D6}\textsuperscript{*7}, \textit{*8}, \textit{*11}, \textit{*13}, \textit{*14}, and \textit{CYP2C19}\textsuperscript{*4}.

\textsuperscript{5} TaqMan copy number variation (CNV) analysis performed for cohort A used assay IDs: Hs00010001\_cn – \textit{CYP2D6} Exon 9, Hs04083572\_cn - \textit{CYP2D6} intron 2, and an RNaseP control. All copy number assays were performed in quadruplicate.

\textsuperscript{6} Ambiguous duplication events were resolved by amplifying the upstream duplicated gene, as described in Gaedigk \textit{et al.}\textsuperscript{190}, and genotyping key allele-defining variants with Sanger sequencing on nested PCR templates.

Predicted metabolizer phenotypes for each participant’s genotype were assigned based on current literature, accessed through the Pharmacogene Variation Consortium website (https://www.pharmvar.org/), in conjunction with the supplemental data available as a companion to the CPIC guideline for \textit{CYP2D6} and \textit{CYP2C19} genotype-guided SSRI dosing\textsuperscript{191}.

For participants taking paroxetine, predicted metabolizer phenotype was assigned based on \textit{CYP2D6} genotype, in accordance with both CPIC and DPWG guidelines (summarized in Table 1.4 on pages 38-40). For participants taking sertraline, citalopram, or escitalopram, predicted metabolizer phenotype was assigned based on \textit{CYP2C19} genotype, again according to CPIC and DPWG guidelines (Table 1.4). Predicted metabolizer phenotype groups were ultra-rapid metabolizer (UM), extensive metabolizer (EM), intermediate metabolizer (IM), and poor metabolizer (PM).
Planned statistical analyses

We planned to summarize demographic variables, EPDS scores, and predicted metabolizer phenotypes descriptively. Standardized daily dose calculations (prescribed daily dose (PDD) / defined daily dose (DDD)\textsuperscript{192}) were planned to enable comparisons across SSRIs. Comparisons between cohort O and cohort A on relevant variables were planned, using parametric or non-parametric tests, as appropriate (based on evaluation of test assumptions in the sample).

Hypothesis testing

To test the main hypothesis, comparison of mean depression scores across the four groups (UM, EM, IM, and PM) was planned using ANCOVA; dependent variable: EPDS mean score, independent (grouping) variable: predicted phenotype group, covariates: standardized SSRI daily dose, weight (kg), and gestational age (weeks). Given the single hypothesis, the threshold for statistical significance was set at $\alpha=0.05$. Data analyses were conducted using SPSS version 25.

Results

Participant characteristics

There were 46 participants from cohort A and 37 from cohort O ($N=83$). There were 28 (33.7%) participants taking paroxetine, 25 (30.1%) taking citalopram, 18 (21.7%) taking sertraline, and 12 (14.5%) taking escitalopram. Average participant age was 31.69 years.
(SD=5.41), and participants were generally highly educated (M=15.91 years of education; SD=2.96).

**Descriptive statistics**

For the whole group, mean total EPDS score was 8.51 (SD=5.56; range: 0 – 29). There were 10 participants with an EPDS score of 15 or more (Table 3.2). A range of EPDS scores were observed across standardized SSRI daily doses (Figure 3.1), and for each metabolizer group (Figure 3.2). In terms of metabolizer phenotype predicted from genotype, the majority of participants were predicted to be extensive metabolizers (n=53; 64%), with 15 predicted to be ultra-rapid metabolizers, 10 predicted to be intermediate metabolizers, and 5 predicted to be poor metabolizers (Table 3.3), which is in line with expectations from similar populations\textsuperscript{128,129}. 


**Table 3.2.** Characteristics of participants scoring above EPDS cut-off for probable major depression in pregnancy (one row per participant)

<table>
<thead>
<tr>
<th>EPDS Score</th>
<th>SSRI taken</th>
<th>Standardized SSRI daily dose</th>
<th>CYP2D6 genotype</th>
<th>CYP2C19 genotype</th>
<th>Predicted metabolizer phenotype</th>
<th>Gestational Age (weeks)</th>
<th>Maternal weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>Paroxetine</td>
<td>0.38</td>
<td>*2/*41</td>
<td>*2/*17</td>
<td>Extensive</td>
<td>33.71</td>
<td>73.80</td>
</tr>
<tr>
<td>17</td>
<td>Paroxetine</td>
<td>0.63</td>
<td>*1/*1</td>
<td>*1/*2</td>
<td>Extensive</td>
<td>34.28</td>
<td>83.25</td>
</tr>
<tr>
<td>17</td>
<td>Citalopram</td>
<td>2</td>
<td>*1/*41</td>
<td>*1/*2</td>
<td>Extensive</td>
<td>32.43</td>
<td>126.10</td>
</tr>
<tr>
<td>17</td>
<td>Sertraline</td>
<td>3</td>
<td>*1/*1</td>
<td>*1/*1</td>
<td>Extensive</td>
<td>36.29</td>
<td>61.69</td>
</tr>
<tr>
<td>18</td>
<td>Sertraline</td>
<td>1</td>
<td>*1/*1</td>
<td>*1/*1</td>
<td>Extensive</td>
<td>37.14</td>
<td>72.57</td>
</tr>
<tr>
<td>18</td>
<td>Escitalopram</td>
<td>1</td>
<td>*1/*4</td>
<td>*1/*1</td>
<td>Extensive</td>
<td>34.14</td>
<td>68.49</td>
</tr>
<tr>
<td>19</td>
<td>Escitalopram</td>
<td>3</td>
<td>*1/*4</td>
<td>*1/*17</td>
<td>Ultra-rapid</td>
<td>37.14</td>
<td>92.99</td>
</tr>
<tr>
<td>22</td>
<td>Escitalopram</td>
<td>1</td>
<td>*1/*1</td>
<td>*1/*1</td>
<td>Extensive</td>
<td>37.57</td>
<td>74.84</td>
</tr>
<tr>
<td>24</td>
<td>Citalopram</td>
<td>2.5</td>
<td>*1/*1</td>
<td>*2/*17</td>
<td>Intermediate</td>
<td>34.43</td>
<td>88.00</td>
</tr>
<tr>
<td>29</td>
<td>Citalopram</td>
<td>1</td>
<td>*1/*4</td>
<td>*1/*1</td>
<td>Extensive</td>
<td>30.00</td>
<td>85.28</td>
</tr>
</tbody>
</table>
**Figure 3.1.** Depression (EPDS) scores across standardized SSRI daily doses

**Figure 3.2.** Depression (EPDS) scores for each predicted metabolizer group: 0 = PM; 1 = IM; 2 = EM; 3 = UM
Table 3.3. Summary of genotype results and predicted metabolizer phenotypes (N=83)

<table>
<thead>
<tr>
<th>Number of participants with combined genotype</th>
<th>CYP2D6 genotype (star alleles)</th>
<th>CYP2C19 genotype (star alleles)</th>
<th>SSRI taken (if relevant)</th>
<th>Predicted metabolizer phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>*1/*2</td>
<td>*2/*2</td>
<td>Citalopram</td>
<td>Poor</td>
</tr>
<tr>
<td>1</td>
<td>*4/*41</td>
<td>*2/*2</td>
<td>Citalopram</td>
<td>Poor</td>
</tr>
<tr>
<td>1</td>
<td>*4/*4</td>
<td>*1/*17</td>
<td>Paroxetine</td>
<td>Poor</td>
</tr>
<tr>
<td>1</td>
<td>*4/*5</td>
<td>*1/*2</td>
<td>Paroxetine</td>
<td>Poor</td>
</tr>
<tr>
<td>1</td>
<td>*10/*36+10</td>
<td>*2/*2</td>
<td>Sertraline</td>
<td>Poor</td>
</tr>
<tr>
<td>1</td>
<td>*1/*1</td>
<td>*1/*2</td>
<td>Sertraline</td>
<td>Intermediate</td>
</tr>
<tr>
<td>1</td>
<td>*1/*1</td>
<td>*2/*17</td>
<td>Citalopram</td>
<td>Intermediate</td>
</tr>
<tr>
<td>1</td>
<td>*1/*5</td>
<td>*1/*2</td>
<td>Escitalopram</td>
<td>Intermediate</td>
</tr>
<tr>
<td>1</td>
<td>*2/*3</td>
<td>*1/*2</td>
<td>Citalopram</td>
<td>Intermediate</td>
</tr>
<tr>
<td>1</td>
<td>*4/*10</td>
<td>*1/*17</td>
<td>Paroxetine</td>
<td>Intermediate</td>
</tr>
<tr>
<td>1</td>
<td>*4/*41</td>
<td>*2/*17</td>
<td>Intermediate</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>*4/*41</td>
<td>*1/*17</td>
<td>Paroxetine</td>
<td>Intermediate</td>
</tr>
<tr>
<td>1</td>
<td>*4/*4</td>
<td>*1/*2</td>
<td>Escitalopram</td>
<td>Intermediate</td>
</tr>
<tr>
<td>1</td>
<td>*4/*4</td>
<td>*2/*17</td>
<td>Citalopram</td>
<td>Intermediate</td>
</tr>
<tr>
<td>1</td>
<td>*5/*9</td>
<td>*1/*1</td>
<td>Paroxetine</td>
<td>Intermediate</td>
</tr>
<tr>
<td>8</td>
<td>*1/*1</td>
<td>*1/*1</td>
<td>Extensive</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Unknowna</td>
<td>*1/*1</td>
<td>Escitalopram</td>
<td>Extensive</td>
</tr>
<tr>
<td>1</td>
<td>*1/*1</td>
<td>*1/*2</td>
<td>Paroxetine</td>
<td>Extensive</td>
</tr>
<tr>
<td>3</td>
<td>*1/*1</td>
<td>*1/*17</td>
<td>Paroxetine</td>
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<td>2</td>
<td>*1/*2</td>
<td>*1/*2</td>
<td>Paroxetine</td>
<td>Extensive</td>
</tr>
<tr>
<td>8</td>
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</tr>
<tr>
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<td>*1/*2</td>
<td>Paroxetine</td>
<td>Extensive</td>
</tr>
<tr>
<td>1</td>
<td>*1/*4</td>
<td>*1/*17</td>
<td>Paroxetine</td>
<td>Extensive</td>
</tr>
</tbody>
</table>

*Positive for the deletion, CYP2D6*5, but heterozygous for the *10 defining variant (rs1065852: A/G). Same result on repeat analysis. No further analysis attempted, given that participant taking escitalopram.
<table>
<thead>
<tr>
<th>Number of participants with combined genotype</th>
<th>CYP2D6 genotype (star alleles)</th>
<th>CYP2C19 genotype (star alleles)</th>
<th>SSRI taken (if relevant)</th>
<th>Predicted metabolizer phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>*1x2/*4</td>
<td>*1/*1</td>
<td></td>
<td>Extensive</td>
</tr>
<tr>
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<td>*1/*1</td>
<td></td>
<td>Extensive</td>
</tr>
<tr>
<td>2</td>
<td>*1/*9</td>
<td>*1/*1</td>
<td></td>
<td>Extensive</td>
</tr>
<tr>
<td>1</td>
<td>*1/*10</td>
<td>*1/*2</td>
<td></td>
<td>Extensive</td>
</tr>
<tr>
<td>1</td>
<td>*1/*10</td>
<td>*2/*2</td>
<td>Paroxetine</td>
<td>Extensive</td>
</tr>
<tr>
<td>4</td>
<td>*1/*41</td>
<td>*1/*1</td>
<td></td>
<td>Extensive</td>
</tr>
<tr>
<td>1</td>
<td>*1/*41</td>
<td>*1/*17</td>
<td>Paroxetine</td>
<td>Extensive</td>
</tr>
<tr>
<td>2</td>
<td>*2/*2</td>
<td>*1/*1</td>
<td></td>
<td>Extensive</td>
</tr>
<tr>
<td>1</td>
<td>*2/*4</td>
<td>*1/*1</td>
<td></td>
<td>Extensive</td>
</tr>
<tr>
<td>1</td>
<td>*2/*10</td>
<td>*2/*2</td>
<td>Paroxetine</td>
<td>Extensive</td>
</tr>
<tr>
<td>3</td>
<td>*2/*41</td>
<td>*1/*1</td>
<td></td>
<td>Extensive</td>
</tr>
<tr>
<td>1</td>
<td>*2/*41</td>
<td>*2/*17</td>
<td>Paroxetine</td>
<td>Extensive</td>
</tr>
<tr>
<td>1</td>
<td>*4/*41</td>
<td>*1/*1</td>
<td></td>
<td>Citalopram</td>
</tr>
<tr>
<td>1</td>
<td>*10/*10</td>
<td>*1/*2</td>
<td>Paroxetine</td>
<td>Extensive</td>
</tr>
<tr>
<td>1</td>
<td>*41/*41</td>
<td>*1/*2</td>
<td>Paroxetine</td>
<td>Extensive</td>
</tr>
<tr>
<td>3</td>
<td>*4/*4</td>
<td>*1/*1</td>
<td></td>
<td>Sertraline</td>
</tr>
<tr>
<td>1</td>
<td>*4/*9</td>
<td>*1/*1</td>
<td></td>
<td>Sertraline</td>
</tr>
<tr>
<td>1</td>
<td>*1/*1</td>
<td>*1/*17</td>
<td>Citalopram</td>
<td>Ultra-rapid</td>
</tr>
<tr>
<td>1</td>
<td>*1/*1</td>
<td>*17/*17</td>
<td>Citalopram</td>
<td>Ultra-rapid</td>
</tr>
<tr>
<td>7</td>
<td>*1/*4</td>
<td>*1/*17</td>
<td>Citalopram/ Escitalopram/ Sertraline</td>
<td>Ultra-rapid</td>
</tr>
<tr>
<td>1</td>
<td>*1/*6</td>
<td>*1/*17</td>
<td>Citalopram</td>
<td>Ultra-rapid</td>
</tr>
<tr>
<td>1</td>
<td>*1/*9</td>
<td>*1/*17</td>
<td>Citalopram</td>
<td>Ultra-rapid</td>
</tr>
<tr>
<td>1</td>
<td>*2/*4</td>
<td>*1/*17</td>
<td>Sertraline</td>
<td>Ultra-rapid</td>
</tr>
<tr>
<td>Number of participants with combined genotype</td>
<td>CYP2D6 genotype (star alleles)</td>
<td>CYP2C19 genotype (star alleles)</td>
<td>SSRI taken (if relevant)</td>
<td>Predicted metabolizer phenotype</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>--------------------------------</td>
<td>--------------------------------</td>
<td>--------------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>1</td>
<td>*2/*5</td>
<td>*1/*17</td>
<td>Citalopram</td>
<td>Ultra-rapid</td>
</tr>
<tr>
<td>1</td>
<td>*2/*10</td>
<td>*1/*17</td>
<td>Sertraline</td>
<td>Ultra-rapid</td>
</tr>
<tr>
<td>1</td>
<td>*4/*41</td>
<td>*17/*17</td>
<td>Sertraline</td>
<td>Ultra-rapid</td>
</tr>
</tbody>
</table>

**Comparisons between groups**

There were no significant differences between cohort A and cohort O for maternal age, years of education, maternal weight, or standardized daily dose. Participants in cohort A were at an earlier gestational age on average (cohort A: $M=30.65$ weeks; cohort O: $M=34.31$ weeks; $t(49.98)=3.75, p<.001$). Participants in cohort A also had a significantly higher EPDS score on average (cohort A: $M=9.74$; cohort O: $M=6.97$; $t(79.17)=-2.40, p=.019$). Cohort A had proportionally more ultra-rapid metabolizers, while cohort O had proportionally more poor metabolizers ($p=.038$, Fisher’s Exact Test). Cohort A had proportionally more participants taking citalopram and escitalopram, while cohort O had proportionally more participants taking paroxetine ($p=.003$, Fisher’s Exact Test).

Data were examined for assumptions underlying ANCOVA, and all variables of interest were found to violate the assumption of normality. Further, none of the covariates of interest correlated with EPDS score (covariates should be continuous, measured reliably, and correlate strongly with the dependent variable). Therefore, the non-parametric alternative to ANOVA, the Kruskal-Wallis Test, was used. The assumptions underlying the Kruskal-Wallis Test (random samples, independent observations, and homogeneity of variances) were not violated. There was no statistically significant difference between EPDS scores across the four predicted phenotype
groups (H(3)= .73, p=.87), with median scores of 7 for the poor metabolizer group, 8 for the intermediate and extensive metabolizer groups, and 6 for the ultra-rapid metabolizer group (Table 3.4; Figure 3.3). Subsequent exploratory analyses revealed no significant differences between predicted metabolizer phenotype groups for standardized daily dose (H(3)= 1.88, p=.60), maternal weight (H(3)= .67, p=.88), or gestational age (H(3)= 2.86, p=.41). There was also no statistically significant difference between EPDS scores across the four predicted phenotype groups for either cohort individually (Cohort A: H(2)= .90, p=.64; Cohort O: H(3)= .95, p=.81).
Table 3.4. EPDS total score, standardized SSRI daily dose, maternal weight, and gestational age for each predicted phenotype group (N=83)

<table>
<thead>
<tr>
<th>Predicted Phenotype Group</th>
<th>EPDS total score (Mean, SD)</th>
<th>Standardized SSRI daily dose (PDD/DDD; Median)</th>
<th>Maternal weight (kg; Mean, SD)</th>
<th>Gestational age (weeks; Mean, SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor Metabolizer (n=5)</td>
<td>7.00 (2.55)</td>
<td>1.5</td>
<td>78.61 (14.08)</td>
<td>34.17 (1.37)</td>
</tr>
<tr>
<td>Intermediate Metabolizer</td>
<td>8.80 (6.55)</td>
<td>1.5</td>
<td>75.88 (15.90)</td>
<td>31.11 (6.19)</td>
</tr>
<tr>
<td>(n=10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extensive Metabolizer</td>
<td>8.87 (5.91)</td>
<td>1.5</td>
<td>77.85 (12.44)</td>
<td>32.29 (5.31)</td>
</tr>
<tr>
<td>(n=53)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultra-rapid metabolizer</td>
<td>7.53 (4.45)</td>
<td>1.0</td>
<td>82.27 (10.19)</td>
<td>32.41 (5.04)</td>
</tr>
<tr>
<td>(n=15)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 3.3. Mean depression (EPDS) scores (95% CI), for each predicted metabolizer group, subdivided into standardized SSRI daily dose categories: <1, 1, and >1
Discussion

This is the first study of pharmacogenetic variations in relation to depression symptoms and citalopram, escitalopram, and sertraline use in pregnancy, highlighting the dearth of research connecting genotype to phenotype within the context of SSRI use in pregnancy. We did not replicate the results of the only previous study evaluating pharmacogenetic variants in relation to depression symptoms and the use of paroxetine in pregnancy, which observed a difference in depression symptoms for \textit{CYP2D6} “fast metabolizers” compared to “slow metabolizers”, with increasing depression symptoms during pregnancy for \textit{CYP2D6} “fast metabolizers” and stable depression symptoms for “slow metabolizers”. It is important to note, however, that the subset of our participants taking paroxetine and \textit{CYP2D6} was much smaller (\(n=28\)) compared to the previous study (\(N=74\)). The previous study also obtained data at three prenatal time-points, and so were able to make comparisons of genotype, EPDS scores and plasma paroxetine concentrations across pregnancy. Finally, the previous study controlled for potential confounding variables such as maternal weight, cigarette smoking, and co-medication. While this previous study was restricted to only paroxetine and \textit{CYP2D6}, our study also investigated \textit{CYP2C19} and three additional antidepressants: citalopram, escitalopram, and sertraline. It is possible that genetic variations in \textit{CYP2D6} impact paroxetine metabolism in pregnancy, with a corresponding impact on depression symptoms, but that variations in \textit{CYP2C19} do not have the same impact on metabolism of citalopram, escitalopram, and sertraline in pregnancy, and depression symptoms.

There are other possibilities that could explain our finding of no difference between predicted phenotype and EPDS scores. I based our phenotype predictions on available data, synthesized in the CPIC and DPWG guidelines regarding genotype-guided dosing for SSRIs.
However, these guidelines are intended for use in the general, non-pregnant population, and based on evidence using non-pregnant samples. Evidence shows that the CYP450 enzymes function differently during pregnancy\textsuperscript{195}, specifically that pregnancy induces an increase in CYP2D6 activity\textsuperscript{194}, and a decrease in CYP2C19 activity\textsuperscript{196}. Thus, phenotype predictions based on data collected outside the prenatal context are likely not appropriate to apply during pregnancy. There is also insufficient evidence at present to combine genotype information from \textit{CYP2D6} and \textit{CYP2C19} to predict SSRI metabolic phenotype on the basis of genotypes for both genes – even outside the perinatal context. It is possible that differences between EPDS scores would emerge for our sample if it were possible to use a holistic phenotype prediction algorithm incorporating genotype information for all the genes in the SSRI metabolic pathways. However, this algorithm would likely also need to be modified for use in pregnancy, as suggested by pharmacokinetic studies\textsuperscript{197}. In particular, one study evaluated pharmacokinetic changes during pregnancy for citalopram, escitalopram, and sertraline, and corresponding depression symptoms, and found increased metabolism and increased depression symptoms in the third trimester of pregnancy\textsuperscript{143}. The authors suggested that the pregnancy-induced activation of CYP2D6 overrides the pregnancy-induced inhibition of CYP2C19.

It is important to consider not only statistical significance, but clinical significance. Arguably, a score difference of three represents a clinically significant difference on the EPDS, given the recommended postpartum cut-off scores of 13 for major depression and 10 for minor depression\textsuperscript{187}. The largest difference between mean EPDS scores for the four metabolizer groups in our study is 1.87 (between the poor metabolizer and extensive metabolizer groups), which is also not clinically significant by this metric. It is striking, however, that 12% of the sample scored 15 or higher on the EPDS in spite of taking an antidepressant, with the implication that
~7% were experiencing major depression at the time. This is consistent with previous work—a study using the EPDS to assess symptoms of depression amongst women continuing versus discontinuing antidepressants during pregnancy found that 21% of women continuing antidepressants scored above an EPDS cut-off score of 13\textsuperscript{198}. Using this cut-off score for our sample identifies 21% with an EPDS score of 13 or more. It is possible that these women were taking sub-optimal antidepressant doses due to concerns regarding societal expectations to avoid or minimize medication use in pregnancy\textsuperscript{199}. In this case, women are not only taking on the risks associated with antidepressant use in pregnancy, but also the risks associated with depression during pregnancy, and are not benefitting from symptom relief.

It was somewhat surprising that there was no relationship observed between phenotype and standardized daily dose. It would be expected that, through the current clinical gold standard of trial and error, those who were poor metabolizers would have a lower standardized daily dose than extensive metabolizers, and that ultra-rapid metabolizers would have a higher standardized daily dose than extensive metabolizers. However, this may similarly be due to changes in enzyme activity during pregnancy, which cannot be accounted for yet in available evidence. Not only that, prescribed daily dose may be impacted, as mentioned, by societal expectations and stigma, acting to discourage women and clinicians from increasing SSRI dose even in light of increasing depression symptoms during pregnancy.

The difference between mean gestational ages of cohort A compared to cohort O were due to differences in recruitment protocols between the studies. The difference between mean EPDS scores of cohort A compared to cohort O may have been due to a difference in data collection protocol. Cohort O required that participants complete study visits at BC Women’s Hospital and Health Centre, whereas study visits for cohort A participants usually occurred at the
participants’ houses – throughout the Greater Vancouver area. Enabling study participation without requiring travel could have made it easier for participants experiencing more symptoms of depression to participate. Differences in frequency of SSRI taken between cohorts O and A likely reflect a shift in clinical prescribing practices from paroxetine as a more popular choice during recruitment in the time period for cohort O to citalopram/escitalopram as a more popular choice during recruitment in the time period for cohort A. The FDA issued highly publicized warnings regarding the use of paroxetine during pregnancy and risk for cardiovascular defects in late 2005, and use of paroxetine in pregnancy dropped precipitously thereafter, with prevalence of paroxetine prescriptions falling to below 0.1% of population-based samples of pregnant women from 2006 – 2011. Escitalopram was first marketed in Canada in early 2005. The shift over time in relative prevalence of paroxetine prescriptions versus citalopram/escitalopram is likely also the source of the difference between the frequency of poor metabolizers versus ultra-rapid metabolizers for cohort O compared to cohort A. The population of British Columbia is largely Caucasian or Asian, and the prevalence of ultra-rapid metabolizer CYP2D6 genotypes is ~5% for Caucasians and ~2% for Asians (South and East). In contrast, the prevalence of ultra-rapid CYP2C19 genotypes is ~30% for Caucasians, ~20% for South Asians, and ~1% for East Asians. Table 3.3 illustrates that there were no CYP2D6/paroxetine ultra-rapid metabolizers in our sample; all ultra-rapid metabolizer genotypes were in CYP2C19, for women taking sertraline/citalopram/escitalopram.

**Limitations**

Our sample was underpowered; however, our results suggest that any potential differences between groups would be very small. While a larger sample size may have detected a small difference between EPDS scores by group, particularly for paroxetine and CYP2D6, it is
more likely that predictions for metabolizer phenotype (that were based on available data from non-pregnant cohorts) were not appropriate for use during pregnancy. With an improved understanding of CYP2D6 and CYP2C19 enzyme activity in pregnancy, and the impact of different CYP2D6 and CYP2C19 genetic variations on their activity in pregnancy, it would be possible to refine a prediction algorithm and re-test our hypothesis. It is also possible that confounding variables masked the impact of CYP2D6 and CYP2C19 in our sample, such as SSRI dose, maternal weight, cigarette smoking, and co-medication with substances that have competing or interacting impacts on the CYP system. Unfortunately, including these covariates in our analysis was not possible given either violations of the assumptions underlying ANCOVA, or the limitations of secondary data analyses. Further, it is possible that participants may have been miscategorized in terms of predicted phenotype because we did not fully sequence and characterize CYP2D6 and CYP2C19 for all participants. However, the alleles that were not tested for all participants were very rare, and the testing that was completed for all participants was chosen based on observed population allele frequencies (greater than 1% minor allele frequency in one or more in the 1000 Genomes Project major continental population groups). These assays have been validated to ensure 99.5% genotyping accuracy. Given that we compared depression scores between women, grouped by genotype, it was not necessary to restrict our analysis to one ethnic group, so we were able to adopt the more ecologically valid approach of analyzing data from different ethnic groups. This is in contrast to the requirements of case-control gene association studies, where allele frequencies are compared between groups with and without a condition (e.g., depression) under the assumption that alleles occurring more frequently in the group with the condition play a causal role. In these studies, population stratification of alleles by ethnic group can lead to false associations, so single ethnic groups are typically studied.
Chapter 4: Conclusions
This dissertation contributes to the literature the first: 1) comprehensive, substantive grounded theory of women’s DM process regarding antidepressant use during pregnancy; 2) exploration of women’s DM regarding antidepressant use in the second or third trimesters of pregnancy; and 3) evaluation of the impact of pharmacogenetic variations in the genes CYP2D6 and CYP2C19 on depression symptoms during pregnancy for women taking a range of SSRIs.

Mental illness stigma and societal expectations of women during pregnancy clearly played a major role in participants’ DM regarding depression treatment during pregnancy – contributing to difficulty in deciding to take antidepressants, or to a decision not to take antidepressants. Arguably the most dire potential consequence of this combination of stigma and societal expectations is untreated depression, leading ultimately to maternal suicide. Less catastrophic, but still regrettable, are the situations in which women’s untreated depression during pregnancy harms their own health and quality of life, and also the health of their babies. While not taking antidepressants doesn’t necessarily mean that depression is untreated, preliminary evidence from this research suggests that it is more likely.

There was a distinct trend towards participants who were more highly educated, with higher socioeconomic status and access to more resources, being more likely to live in an urban centre, to access private mental health care and other self-management strategies, and to choose to take antidepressants in pregnancy. In contrast, participants with less education and fewer resources were more likely to choose not to take antidepressants during pregnancy, and to be unable to access alternative treatment options for depression. This is surprising, considering that antidepressants are financially and geographically more accessible than most alternative treatments for depression. An explanation for this potentially counter-intuitive finding is that women with educational and socioeconomic privilege both: have access to additional
resources for mental health care; and also are better positioned to overcome stigma in order to make the societally unpopular choice. Consistent with this explanation, Stepanuk et al. found that women in their study who chose to take antidepressants during pregnancy were more aware of, and able to overcome, societal pressure to avoid medication use in pregnancy. On the other hand, participants who chose not to take antidepressants were more susceptible to negative societal attitudes towards medication use in pregnancy.

The near-universal default position for participants was to prioritize the health of their baby over their own health. This is consistent with female gender norms in a patriarchal society that place more value on the health of children relative to the health of women, and expect women to bear the majority of childcare responsibilities. Participants’ need to show themselves that they had behaved responsibly in order to let go of their decision reflected the pressure they felt to demonstrate conscientious behaviour as a (future) mother. Steps they had taken to be proactive, for example, in the preconception period, reinforced their identity as a responsible mother and helped them to accept their decision regarding mental health treatment in pregnancy. Arguably, the burden felt by women making decisions about mental health treatment during pregnancy is another example of the invisible and unpaid emotional work that is expected of women. Health care providers and romantic partners may genuinely feel that they are supporting a woman’s autonomy by giving her control over her treatment decision, but taking no responsibility for the decision also enables them to avoid any future culpability for decisional outcomes. In contrast, women’s acute awareness of the potential outcomes of their decision was usually associated with intense experiences of guilt and anticipation of guilt – particularly when they felt alone in the DM process. This risk of blame for women in the context of a culture that privileges autonomy and self-determination has been observed in media portrayals of women.
and identified specifically with respect to women’s “choice” to delay childbearing\textsuperscript{214}. As other authors have articulated\textsuperscript{215–222}, relational autonomy can strike a good balance between wanting to ensure women have control over decisions related to their bodies, but also the emotional and social support they need.

The emphasis placed by women on medication necessity beliefs and conducting physical experiments to ascertain the ‘lowest possible dose’ of antidepressant for use in pregnancy spotlight the potential enthusiasm with which women are likely to consider pharmacogenomic testing to support their DM. Pharmacogenomic testing could fit within our DM model in the ‘Seeking information’ and ‘Making sense of information’ clusters of DM activities, and it may become a practical reality sooner rather than later as companies offering pharmacogenomic testing become more prominent and active in their marketing efforts. There is thus an urgent need for more research to allow the prediction of phenotype from genotype in light of: 1) the functioning of the enzymes in the metabolic pathways of antidepressants during pregnancy, and 2) the interaction of multiple enzymes (from different pharmacogenes) in the metabolic pathways of antidepressants.

**Clinical implications**

It was evident in this study that health care providers played a significant role in participants’ DM, and that there were many potential opportunities for clinicians to enhance women’s DM experience. Sharing DM with a clinician was cited by many participants as the single most influential factor in their DM process. A key aspect of sharing DM was supporting women to make sense of information and manage their emotions related to the decision; participants consistently reported that providing information and/or advice (for example, in a
paternalistic model of DM) was not sufficient to help them in reaching a decision. This is reflected in the theory diagram; participants did not go straight from seeking information to reaching a decision – it was necessary to make sense of the information and/or self-soothe before reaching a decision. Thus, to support patients in this DM process, it is beneficial for clinicians to join patients in some, or all, of the activities in the ‘making sense of information’ and ‘self-soothing’ clusters of DM activities.

Some of these DM activities are especially worthy of highlighting for consideration by clinicians: the impact of the quality of their relationship/interaction on patient appraisals of information trustworthiness; reflections on medication necessity beliefs in relation to evaluations of risks of harm; use of language and its impact on risk perception; and the potential for self-soothing strategies and/or tactics for ‘living with the decision’ to help women reach and/or accept a decision. Participants were more likely to trust information from clinicians if they perceived the clinicians’ information-sharing to be: frank, tailored to their situation, and non-judgemental. As seen in our study, there is a significant risk if providers avoid being frank and withhold information about risks of antidepressants. When women heard about risks later, from another source, their trust in the clinician who had omitted this information was undermined.

Participants were likely to seek information from other sources if they identified a conflict between their beliefs and the information they received from a clinician, or the preferences of their provider. Explicitly exploring women’s beliefs and preferences as part of the DM process could expose assumptions made by both the patient and provider, and then enable clarification. Preliminary evidence from this study suggests that clinicians generally define a threshold of severity at which antidepressants are needed that is lower than that defined by their patients. Further, it seemed in this study that clinicians defined the threshold of what was an
acceptable risk of harm to a baby at a higher level than did patients. These beliefs, acting together, resulted in baseline positions whereby providers were more likely to prefer that patients maintain or initiate antidepressant treatment, and patients were more likely to prefer not to take antidepressants. Thus, it could be helpful for clinicians to deliberately open a dialogue about how their patients would define when antidepressants are needed and the possible impact, from the provider’s perspective, of different thresholds of severity that patients might use for making this decision.

When providers used stigmatizing language, it was quite influential on participants’ DM. A noteworthy example was the use of the word ‘withdrawal’ in the context of neonatal abstinence syndrome when women took antidepressants in pregnancy. Participants associated withdrawal with substance use, which is highly stigmatized, and this language elevated women’s perceptions of risk of harm to their baby. Painting a picture of what neonatal abstinence syndrome actually means helped lower risk perception. Data from this study suggests that it would be valuable for providers to generally make a point of incorporating into interactions with patients translations of clinical labels into concrete expectations for corresponding ‘real world’ experiences.

Providers could consider sharing with their patients the self-soothing strategies that participants in this study used during DM. In particular, if providers notice patients engaging in thought experiments, they could consider working with their patients to develop a mantra, given that women in this study found repeating a mantra helpful in combatting the anxiety induced by thought experiments. For women with particularly high anxiety (perhaps with a diagnosed anxiety disorder), the tactics used by participants in this study to ‘try to live with the decision’
could be especially valuable for use in breaking a cycle of anxiety-fueled information seeking, and accepting a decision.

Results from this dissertation do not support the clinical use of pharmacogenomic testing for antidepressant use during pregnancy. It would be ideal to see the practice guidelines for CYP2D6/CYP2C19-guided SSRI dosing revised to specify that there is insufficient evidence at this time for their application in the pregnant population. Regardless, it is important for providers to be aware that women might seek this testing from the companies that offer it directly to consumers. Providers could proactively explore women’s illness and medication necessity beliefs and share what is currently known regarding the causes of perinatal depression, ideally referring to a psychiatric genetic counsellor to best support this discussion223. Further, providers could consider sharing information about available direct-to-consumer pharmacogenomic testing, along with current limits regarding its interpretation and clinical application.

Our findings also have implications for the healthcare system more broadly. In particular, our study highlights issues related to access – including inequities across the population, and inconsistencies between providers within the system. The issue of waitlists for accessing specialist providers was mentioned repeatedly, and has potentially significant consequences in the context of inconsistent messaging between primary care providers and specialist providers. Preliminary evidence from our study suggests that primary care providers are more likely to recommend or support patients in stopping antidepressants for pregnancy, but without a comprehensive conversation about the implications of this choice for women and their babies. Unfortunately, if primary care providers did make a referral to a reproductive psychiatrist (which was not always the case), waitlists resulted in patients being seen months later – often around the time of delivery - and participants in this study were unwilling to change their decision at that
point. Especially given the recent closure of the Motherisk phone lines in May 2019\textsuperscript{224}, there is an urgent need to provide an alternate pathway to accessing evidence-based information (and ideally, counselling) as soon as women begin DM. Digital health interventions show great promise as a way to connect women with evidence-based information, and there is work already in this area on which to build\textsuperscript{225}.

In summary, the grounded theory provides insight into how women have made decisions about how to care for their mental health during pregnancy, which can be useful both practically and emotionally for other women approaching this DM process, and their providers. Evidence from the pharmacogenetic study clarifies the limitations of this field, which is especially vital in this era of direct-to-consumer genetic testing. Together, they can support patient-oriented decision making regarding perinatal maternal mental health.

**Future directions**

Towards the broader goal of supporting women making decisions about how to care for their mental health during pregnancy, there is a need for not only further research, but also knowledge dissemination/exchange.

In terms of further research, both the qualitative and quantitative studies revealed promising avenues for exploration. While there have been numerous meta-analyses of quantitatively- and clinically- measured infant outcomes (and a few of maternal outcomes) for women who took antidepressants during pregnancy, as well as some for women with untreated depression during pregnancy, there are no studies (of which we are aware) that investigate and portray women’s experiences of these outcomes. Given the interest from all participants in hearing stories from other women about what these clinical labels mean in the real world, and the
way some women were able to use this information to lower their anxiety during DM, it would be beneficial to conduct further qualitative investigations into this area. Similarly, future work could elaborate on how women perceive these various risks associated with either antidepressants or untreated depression during pregnancy, and how clinicians could support women in risk perception and management. Preliminary evidence from the participant follow-up interviews suggests that women would find our model useful during DM, and it would be valuable to assess the impact of integrating the model into clinical settings on women’s DM process and outcomes. Further, it would be interesting to build on this substantive grounded theory in the development of formal grounded theories to describe DM in: 1) women’s mental health, and 2) pregnancy.

Preliminary evidence from the interview study indicates that women with a history of depression would be very attracted to pursuing pharmacogenetic testing if it were to become part of clinical care, but it would be valuable for future research to explore women’s perspectives regarding pharmacogenetic testing in this context. A great deal of further research is needed before pharmacogenomic testing can hope to offer women guidance for the personalization of antidepressant medication choice and dose during pregnancy. Historically, clinical trials evaluating antidepressant medications have not prioritized the inclusion of women, and – in fact – have specifically excluded pregnant women. Thus, our knowledge of the function of antidepressants in pregnant women is woefully inadequate. Even our knowledge of the function of antidepressants in general populations does not currently allow for combining results of pharmacogenomic testing of different genes, such as CYP2D6 and CYP2C19, in a holistic phenotype prediction algorithm. Avenues for future research include: the impact of pharmacogenomic variants of multiple genes together on phenotype; the function of enzymes
relevant to antidepressant function during pregnancy; the function of metabolic pathways responsible for antidepressants other than SSRIs and their relationships to underlying genomic variation; and the impact of pharmacogenomic variants (via metabolic activity) on maternal and infant outcomes, including for women taking multiple antidepressants at the same time.

Feminist research is often recognized to be both scientific and political, and to share an underlying motivation to improve the conditions of women’s lives. Given this, and the feminist research principle of minimizing the power differential between researcher and participant, it is particularly important to the integrity of research conducted within a feminist paradigm to share results with participants, and women more broadly. Knowledge dissemination/exchange thus represents a crucial next step for this research. Preliminary discussions with some of the participants regarding directions for knowledge dissemination and exchange were initiated during the qualitative study follow-up interviews. Possible future avenues include: the development of a patient-facing website incorporating women’s stories and the DM model; the translation of the model into video format (to be available online); and the development of clinical practice guidelines and tools to support clinicians to incorporate insights from this research into the care they provide to women.
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Appendices

Qualitative study

Appendix I: Demographics questionnaire
Appendix II: Initial interview guide (version 1)
Appendix III: Follow-up interview guide (version 1)
Appendix IV: Results summary sent to participants before follow-up interviews

Quantitative study

Appendix V: The Edinburgh Postnatal Depression Scale (EPDS)
Qualitative study

Appendix I: Demographics questionnaire

SECTION A

How old are you? (open response)

Are you currently in a committed relationship? Yes/No

Have you ever experienced depression?
   Yes, I have received a diagnosis of depression
   Yes, but I wasn’t formally diagnosed
   No

Have you ever discussed taking an antidepressant with a health care provider? Yes/No
   If yes:
      Have you discussed taking an antidepressant with a health care provider within the past six months?

Have you ever taken an antidepressant? Yes/No
   If yes:
      Have you taken an antidepressant within the last six months? Yes/No
      Are you currently taking an antidepressant? Yes/No

Are you currently pregnant? Yes/No/Unsure

< Branch logic >

SECTION B1 (only completed by those currently pregnant)

What is your due date? (select from calendar)

Was this a planned pregnancy (select the best option)?
   - I was actively trying to conceive
   - I had stopped trying not to conceive
   - It was in my plans to become pregnant at some point, but I was still using some form of birth control
   - I was not planning to become pregnant at this time
   - I was not planning to become pregnant at any point
How was the baby conceived?
- Naturally
- In vitro fertilization (IVF)
- IVF/Intracytoplasmic sperm injection (ICSI)
- Other fertility treatments

What health professionals have cared for you during your pregnancy so far?
- Family practice physician
- Midwife
- Doula
- Genetic Counselor
- OBGYN
- Psychiatrist
- Psychologist
- Other (open response)

Have you taken any medication during the pregnancy (even for a short time, for example, before finding out you were pregnant)? Yes/No

If Yes:
What medications have you taken?
- Medication for depression – please specify:
- Medication for mania or psychosis – please specify:
- Medication for nausea – please specify:
- Medication for pain – please specify:
- Other (open response)

Is this your first pregnancy? Yes/No

If No:
How many pregnancies have you had in the past? (open response)
Have you experienced depression during a previous pregnancy? Yes/No
Have you taken an antidepressant during a previous pregnancy? Yes/No

< End of questionnaire - Thank you page >

SECTION B2 (only completed by those not currently pregnant)

Are you planning to become pregnant in the next year? Yes/No

If yes:
Are you planning to take an antidepressant during the pregnancy?
- Yes, I most likely will take an antidepressant during the pregnancy
- No, I most likely will not take an antidepressant during the pregnancy
- I haven’t decided yet whether or not I will take an antidepressant during the pregnancy

Have you been pregnant before? Yes/No

If yes:
  How many pregnancies have you had in the past? (open response)
  Have you experienced depression during a previous pregnancy? Yes/No
  Have you taken an antidepressant during a previous pregnancy? Yes/No

< End of questionnaire - Thank you page >
Appendix II: Initial interview guide (v1)

*Introduce yourself to the interviewee.*

Thank you for agreeing to participate in this research study. As you know, we are interested in learning about how women decide whether or not to take antidepressants during pregnancy.

Have you had a chance to review the consent form? Do you feel that you have had enough time to consider participating? Do you have any questions about the consent form or about participating?

I would like to emphasize that all of the information that you provide will be kept confidential and that your participation is voluntary, which means that you can stop at any time, feel free to ask for clarification, and/or decide not to answer any or all of the questions. I also just want to remind you that participating in this study in no way waives any legal rights that you have, or changes any care or services that you may be receiving.

Would you confirm for me whether you would like to participate?

If yes – continue; if no – thank you very much for your time.

**Introduction:**

I will be recording the interview, and will start by asking you some questions about your experience of healthcare decision making generally, then questions about your experience of depression and treatment for depression outside the context of pregnancy, followed by questions related to treatment for depression during pregnancy. The interview will take approximately sixty (60) minutes. Please feel free to ask to pause the recording at any point in the interview should you require a break. At the beginning of the recording, I will announce your participant ID to keep your identity confidential. If you can avoid using names during the interview, that will also help, but don’t worry if you happen to use one because we will remove it at the time of transcription.

*Ask whether she has any questions about the interview process before you begin, then begin the interview. Prompt where necessary and ensure that the main questions below are addressed. Prompts are in italics below each question. Probes aim to open up conversation to gain a deeper understanding of the primary questions and issues of importance to participants. As such, effort will be made to frame these prompts as open-ended questions. The way probes are written in this guide are simply examples and there is flexibility for exact wording in the interviews. It is not necessary to ask all probes.*
Section A. General experiences of healthcare decision-making

Prompt where necessary and ensure that the main questions below are addressed. Prompts are in italics below each question. It is not necessary to ask all probes.

So, as I mentioned, I’ll start by asking some questions about your experience of healthcare decision making generally.

Can you tell me a bit about your approach to your healthcare generally?
  *What has been your experience when you have had a health concern? (self-management, go to the doctor, hope it goes away on its own)*
  *How do you feel about taking medications generally (e.g. for headaches/colds/flus)?*
  *Can you please share your thoughts about preventive medicine (e.g. vaccinations, wellness strategies like exercise and a good sleep routine)?*
  *Has your cultural or family background influenced your attitudes towards how to approach health concerns? If so, in what ways?*

Could you please share how you’ve approached making decisions about your healthcare?
  *Can you think of examples of times when treatment options have been presented to you?*
  *Could you please share one with me?*
  *What was your experience of then making the decision? Could you describe your process (e.g. using logic and information or emotion and intuition)? Who did you talk to about the decision and how did you decide who to talk to about the decision?*

Section B. General experiences of treatment decision-making for depression

Prompt where necessary and ensure that the main questions below are addressed. Prompts are in italics below each question. It is not necessary to ask all probes.

So now let’s move to questions about your experience of depression and treatment for depression outside the context of pregnancy.

Could you please share with me a little about your experience of depression?
  *When have you been depressed?*
  *What was happening in your life at that time?*
  *How long were you depressed?*

What has been your experience related to treatment for depression?
  *What has been your experience related to antidepressants?*
  *What other treatment options have you tried or considered?*
  *What positive experiences have you had with treatment options for depression? Negative experiences?*
  *How have you learned about treatment options for depression? From healthcare providers? Friends? Family? Internet research?*
How much control do you feel that you have when it comes to your mental health?

Do you feel like it’s something you have the power to influence or do you feel helpless to prevent episodes of mental illness?

How have you decided on treatment approaches for depression?

Could you describe your process (e.g. using logic/information or emotion/intuition)?

How involved have you been in the decision-making process? Have you taken on an active role (primary responsibility for decisions)? Collaborative role? Passive role (primary responsibility is someone else’s)?

What has been your experience re: voluntary treatment/involuntary?

How much control do you feel that you have had in decisions about treatment for your mental health?

How have treatment options been presented to you? By whom?

Who have you talked to about treatment decisions? How did that go?

What things have you found helpful in deciding on treatment options for depression (e.g. having access to latest evidence, having support from doctor/friends/family, having space and time to consider, hearing what has worked for other people)? What things have you found make decision-making about treatment options for depression more difficult (e.g. symptoms of depression, fear of change, lack of acceptance of illness, lack of support from doctor/friends/family, lack of info)?

Would you say that your mood impacts your decision-making? If so, in what ways? Are there different things that you find helpful in decision-making when you’re experiencing depression as compared to when you aren’t? Are there different things that make decision-making more difficult?

What factors have you considered when deciding on treatment approaches for depression?

Medication side effects
Past experience with treatments/healthcare providers
Doubts about effectiveness of treatment option(s)
General attitudes/beliefs about cause of illness/approach to treatment (culturally, family background)
Support from family/friends/health care providers
Consequences of trying a treatment option? And of not trying a treatment option?
Cost of treatment option(s)

How did you perceive risks associated with treatment option(s) (including no treatment)?

High/low? Can you put a number(s) on it? Could you share more about how this impacted your decision-making?

Could you tell me more about emotions you experience when considering changes in your approach to caring for your mental health (e.g. fear? optimism)?
How do you feel about your decision(s) about mental health treatment?
  Have you felt anxious about your decision(s)?
  Have you felt confident about your decision(s)?
  How much have you continued to think about decision(s) after you’ve made them?
  What things have helped you feel good about your decision(s) (if any)?
  What things have made you doubt your decision(s) (if any)?

Section C: Treatment decision-making for depression in pregnancy

Prompt where necessary and ensure that the main questions below are addressed. Prompts are in italics below each question. It is not necessary to ask all probes.

We’re now going to turn our attention to the final section of questions related to treatment for depression during pregnancy.

Could you please tell me about your experience of deciding whether or not to take antidepressants during pregnancy?
  Have you already made a decision or are you still deciding?
  Please describe how you approached/are approaching the decision (e.g. using logic and information or emotion and intuition)?
  Did you make a decision and then change your mind?
  Who have you talked to about treatment decisions? How did that go?
  How have treatment options been presented to you (if applicable)? By whom?
  Could you tell me more about that experience/interaction?
  How involved have you been in the decision-making process? Have you taken on an active role (primary responsibility for decisions)? Collaborative role? Passive role (primary responsibility is someone else’s)?
  How much control did you/do you feel that you had/have in the decision about whether to take antidepressants during pregnancy?
  What things have you found helpful in deciding on treatment options for depression (e.g. having access to latest evidence, having support from doctor/friends/family, having space and time to consider, hearing what has worked for other people)? What things have you found make decision-making about treatment options for depression more difficult (e.g. symptoms of depression, fear of change, lack of acceptance of illness, lack of support from doctor/friends/family, lack of info)?

What was your process of reflecting on the decision of whether or not to take antidepressants during pregnancy?
  Did you/do you feel like you had/have a good understanding of the possible consequences/outcomes of the different treatment options (how confident are you in your understanding of the possible consequences/outcomes of the different treatment options)?
  If you have you avoided thinking about the decision, what would you say are the reasons for this avoidance?
  Have you spent time researching treatment options and outcomes? If so, how have you sought this information?
What factors have you considered when deciding on treatment approaches for depression during pregnancy?

- Medication side effects
- Past experience with treatments/healthcare providers
- Doubts about effectiveness of treatment option(s)
- Support from family/friends/health care providers
- Consequences of trying a treatment option? And of not trying a treatment option?
- Cost of treatment option(s)
- Impact of treatment options (including no treatment) on the baby

How did you perceive risks associated with treatment option(s) – for yourself and the baby? High/low? Can you put a number(s) on it? Could you share more about how this impacted your decision-making?

What would be your ‘worst case scenario? Your best case scenario? How much control did/do you feel that you have to achieve your best case scenario/avoid your worst case scenario?

Do you know of anyone who has had depression prior to pregnancy who decided how to manage their mental health during pregnancy? If so, what kind of experience did they have? Did this influence your decision?

Have you felt pushed in one direction or another by others’ opinions/the attitudes of society?

- How do you feel others view women who take antidepressants during pregnancy?
- What has been your experience of how others have viewed your decisions about mental health treatment? During pregnancy/outside of pregnancy?
- What has been the reaction of your family or friends regarding your decisions about mental health treatment? During pregnancy/outside of pregnancy?
- How comfortable are you in telling people about your mental health care choices?
- How have others’ views impacted your decision-making about treatment options?

What was/has been most influential in your decision making process?

How do you feel about your decision(s) about mental health treatment during pregnancy?

- Have you felt anxious about your decision?
- Have you felt confident about your decision?
- How much have you continued to think about your decision after you made it?
- What things have helped you feel good about your decision?
- What things have made you doubt your decision?

When you think about the treatment decision-making for depression you did before pregnancy/planning for pregnancy compared to what we just discussed about treatment decision-making for depression during pregnancy/planning for pregnancy, how do you feel like they were different?

- How has being pregnant influenced how you perceive your treatment choice(s)? How has being pregnant made your decision easier? More difficult?
Are there things that have been helpful or that would be helpful in caring for your mental health in pregnancy? Could you tell me more?

If pregnant – have you had any pregnancy complications? Have they affected your mental health? Have they affected your decisions about treatment for your mental health?

Is there anything else you would like to add (perhaps that you’ve been thinking about but haven’t had the chance to share)?

**Conclusion:**

Thank you so much for your contributions to research. I will be continuing to conduct interviews for approximately the next *<insert estimate here>* months, and will be analyzing the interviews as I go along. It’s possible that when I review our interview, I may have some questions to clarify that I’ve understood your perspective. If I do, would it be ok for me to contact you again with these questions?

Given that you have generously offered your time to participate in this study, we wonder if you would be interested in participating in any other current studies, or possibly future studies? We would like your permission for a staff member from our center to contact you at some future time. At that time, there would be no obligation to participate in another study. The staff member would simply have permission to make contact with you in order to provide information about a study in which you could participate if you wish. If you do agree to be contacted, you may change your mind at any time without affecting any support or treatment you receive currently. All information you provide will be kept confidential and will not be used for any other purpose than to contact you about research projects that you might be interested in participating in.

Would you be interested in being contacted to hear about other research studies?

Would you be interested in receiving a summary of the study results?

*If participant expressed interest in receiving a summary of the study results:* I will definitely send you the summary of the study results when available. I am hoping that will be approximately *<insert estimate here>*.

I would like to send you the small thank you for your time today, so could I please take down your mailing address?

Thank you so much again, and I wish you all the best.
Appendix III: Follow-up interview guide (v1)

Intro blurb items to mention:
- I’ll be recording our conversation
- Same as last time, at the beginning of the recording, I’ll announce your participant ID to keep your identity confidential.
- This conversation should only take about 15 – 20 minutes or less, but please let me know if you need me to pause the recording if something comes up in the background that needs your attention.
- Any questions?

*Only probe a lot if someone says that something doesn’t capture their experience.*

1. What did you think of the results? (big picture, gut reaction)
2. Did the results fit with your experience? Anything that was important for you that was missing?
3. Were there any things that didn’t sit right for you?
4. Did anything trigger an emotional reaction for you? (chance to debrief)
5. Anything else you’d like to add?
6. Anything you’d like to ask me?

I’ll be incorporating feedback from yourself and others into the results over the next month or so, and hope to finalize the results by the end of August. I may not be able to send you the final summary until later, though, because I’m expecting baby # 2 in October and baby # 1 made his appearance early! I will send you the results when I can, though.

Thank you so much, again, for your support of my research!
Appendix IV: Results summary sent to participants before follow-up interviews
Decision making about mental health care during pregnancy: A woman-centred theoretical model

- **Blue circle**: The decision-making process
- **White box with solid black outline**: System-level factors underlying, and influencing, the decision-making process
- **Shapes with dotted outlines** (purple & white circles, & white boxes for emotions): Transitory states influencing movement within the decision-making process
- **Solid gray circles**: clusters of decision-making activities
- **Gray/black arrows**: Processes connecting clusters of activities to each other (gray) or to the outcome of decision-making (black)
- **Purple/white arrows**: Possible starting points from which participants entered the decision-making process (stage in perinatal period or from a decision)
Through my interviews with 31 women, I co-created this woman-centred model of decision-making to represent the experience of deciding whether or not to take antidepressants during pregnancy. Women deciding about taking antidepressants during pregnancy also considered the broader question of how to care for their mental health more generally during the perinatal period. The perinatal period includes the time before conceiving, during pregnancy, and the postpartum.

The woman in the centre of the model has experienced depression, and she is either pregnant or planning a pregnancy. The blue circle represents the decision-making process. The large purple circle surrounding the woman and the decision-making process represents the perinatal period. At any time during pregnancy planning (preconception), or pregnancy (1st – 3rd trimester), women may visit or re-visit decision-making about how to care for their mental health in pregnancy. This is represented by the purple arrows going from the perinatal period circle into the decision-making process circle.

The large square box around the whole model symbolizes the societal context in which women make decisions about antidepressant use in pregnancy. Societal factors that were discussed in the interviews as being most relevant to the decision-making process were: patriarchy, privilege, societal expectations of pregnancy, and stigma. These impacted decisions about mental healthcare during pregnancy by making it easier or more difficult to access support (e.g., the cost of therapy, lack of services in a given geographic region, feeling like it’s not ok to talk about taking antidepressants or depression during pregnancy for fear of being judged).

*societally, I mean, I’m certainly not immune. We live in a patriarchy. We live in a mother shaming culture, so I certainly ... you know, I have Facebook and I read the news and ... right? I certainly know that that stigma is out there, of antidepressants in pregnancy. – Rebecca

Three emotions – anxiety, guilt, and fear – dominated women’s decision-making process. These emotions came and went, but were powerful factors that influenced how women experienced making these decisions.

*I went into pregnancy saying to myself, ‘This can go two ways. You can either feed the anxiety, and add worry about every single thing you eat, and every pill you take.’ And knowing I’m an anxiety-prone person, I knew that if I started down that road, it would not be good. So, I kind of went into it, with my husband’s support and everything, as I’m going to be as relaxed as possible about medication use, because otherwise it’s just going to be this big ball of guilt, and like what if... what if... what if...? I had to consciously shut that down and say, ‘You’ve made your decision. If something terrible happens, and there’s a defect, yes, that would be terrible’. However, you couldn’t actually ever really say that it was the... like, heart defects are pretty common actually. So, you just have to make the decision, and then deal with whatever. – Jane*
The decision-making process itself was complex and dynamic. There were not separate stages or phases. There were three clusters of activities, which were strongly connected to one another. These clusters were: 1) Seeking Information, 2) Making Sense of Information, and 3) Self-soothing. Decision-making involved moving back and forth between these clusters many times, and in many ways. This is represented by the double gray arrows going in both directions between the smaller gray circles.

In the ‘Seeking Information’ cluster of activities, women sought information about two main topics: 1) risks of harm to themselves, and 2) risks of harm to their baby. Sources of information included: internal reflections (e.g., on past experience); talks with family, friends, or healthcare providers; and written information (including medical websites, blogs, online forums, textbooks, and peer-reviewed literature).

It dawned on me that I knew so little about being pregnant, and I didn’t want to do anything that would harm the baby. I had no idea what to do. I didn’t really have any way of making an informed decision. The walk-in clinic doctor had told me that there was little information about it, and that there is... he said that it’s possible there’s a small chance that it could have an effect on the baby, so he gave me some information to read. But I just decided... I mean, I don’t even know if I read the information, I just decided that... I didn’t like that answer and that chance, hearing that there was a chance, so I... he said it was inconclusive, the research or the studies, but I just decided that I didn’t want to... it wasn’t worth it for me to take that chance at that time, because I was feeling alright anyway. – Vanessa

In the ‘Making Sense of Information’ cluster of activities, women considered whether information was trustworthy, reflected on their beliefs, conducted thought experiments (i.e., imagined what might happen depending on what they chose), explored information from different angles, and integrated information to evaluate risks of harm.

I asked [my reproductive psychiatrist] with – you saw that UBC research that came out on Effexor? [Yes] But she said that’s usually when you’re on 375 or 425 – like, really high doses. And she’s like, “You’re doing okay on a pretty low dose, so just chill here.” But it just makes me sad, because I know what it feels like when I don’t have my pill. I’ve only done it a few times, but you get heart complications and it’s very uncomfortable... because she was saying some babies get the jitters. I’m like, “Oh God!” - you don’t want to think of your baby coming out like a heroin addict baby. That’s the sad part because you’re like – like that sucks when I think of it that way. It sucks. I’m okay with taking a little bit of a risk. It’s different when it’s yourself, like I don’t care about me. You don’t want to bring someone into the world and then them be like, “Why did you do that?” I just don’t want my kid to be like, “My mom was on anti-depressants.” I just don’t want it to actually like affect... I would die if that was the case. I would die. I think that would be the worst thing that could absolutely happen to me is have a baby that was like ill in a
way. I would think it was completely my fault. I would take that on and it would kill me. Yeah, it would kill me for sure. – Desiree

In the ‘Self-soothing’ cluster of activities, women took steps to manage their anxiety, guilt, or fear, to try to ‘get comfortable’ in the process or with a possible decision. Self-soothing activities included: repeating a mantra (e.g., “doing the best I can”); normalizing (i.e., a process of comparing themselves to others in a connection to their common humanity – an expression of self-compassion); gatekeeping (i.e., ways to respond to unsolicited advice or alarming media articles, including filtering them out or limiting information sharing with others); and building a safety net.

I have had a couple of those thoughts, I would say, ‘What if it's really, really bad? What if I have postpartum depression and I can't attach properly to my kid? What if...’ – you know, sort of like going down the bad path. And I'm just trying to stop myself from that and be like, okay - you're preparing yourself, you're going to totally try to do the best that you can -- and not get too wrapped up in those. - Lena

In order to reach a decision, including a decision to defer the decision, women engaged in further decision-making processes to get from the ‘Making Sense of Information’ cluster of activities or the ‘Self-soothing’ cluster to a decision. These processes are represented by the black arrows from those two clusters to the white ‘decision’ circle surrounding the blue decision-making process circle. These processes to reach a decision included: assessing whether information from different sources was consistent and/or fit with their beliefs and preferences; managing any conflict that was identified, assigning weight to information, and efforts to accept a tentative decisional preference.

[The reproductive psychiatrist] said they did another study on it, saying that the birth defects were so mild, it would be more worth it now to give it a go, because the studies that I was reading online were a number of years ago. Apparently they had done a new study, and they said that they weren’t as bad as what they were. So I’m not 100% sure. I’ve had doctors say that it’s fine now. And I’ve got my family doctor saying he still doesn’t want me on it. So I don’t really know what to do. That’s a pretty big risk to take, you know, do I trust in another person and then something ends up happening and then... you know, I’m going to be upset with myself and that person probably for the rest of my life. It’s not really a risk that I feel like I wanna take. – Madison

Reaching a decision wasn’t necessarily final. The white decision circle has a dotted outline to show that it is not a permanent state. Women could return to the decision-making process and either confirm or change their decision later. This is depicted in the diagram with the small white arrow going from the white decision circle into the decision-making process circle.
Quantitative study

Appendix V: The Edinburgh Postnatal Depression Scale (EPDS)
As you are currently pregnant/have just had a baby, we would like to know how you are feeling. Please CHECK the answer which comes closest to how you have felt IN THE PAST 7 DAYS, not just how you feel today. Please complete all ten items. Please complete the scale yourself, unless you have difficulty with reading.

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<tr>
<td>1</td>
<td>I have been able to laugh and see the funny side of things.</td>
<td>As much as I always could</td>
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<td></td>
<td></td>
<td>Not quite so much now</td>
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<td></td>
<td>Definitely not so much now</td>
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<td></td>
<td></td>
<td>Not at all</td>
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<td>2</td>
<td>I have looked forward with enjoyment to things.</td>
<td>As much as I ever did</td>
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<td>Rather less than I used to</td>
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<td></td>
<td></td>
<td>Definitely less than I used to</td>
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<td></td>
<td></td>
<td>Hardly at all</td>
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<tr>
<td>3</td>
<td>I have blamed myself unnecessarily when things went wrong.</td>
<td>Yes, most of the time</td>
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<td>Yes, some of the time</td>
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<td>Not very often</td>
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<td>No, never.</td>
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<td>4</td>
<td>I have been anxious or worried for no good reason.</td>
<td>No, not at all</td>
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<td>Hardly ever</td>
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<td>Yes, sometimes</td>
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<td>Yes, very often</td>
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<td>5</td>
<td>I have felt scared or panicky for no very good reason.</td>
<td>Yes, quite a lot</td>
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<td>Yes, sometimes</td>
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<td></td>
<td></td>
<td>No, not much</td>
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<td></td>
<td>No, not at all</td>
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<td>6</td>
<td>Things have been getting on top of me.</td>
<td>Yes, most of the time I haven't been able to cope at all</td>
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<td>Yes, sometimes I haven't been coping as well as usual</td>
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<td></td>
<td>No, most of the time I have coped quite well</td>
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<td></td>
<td></td>
<td>No, I have been coping as well as ever</td>
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<td>7</td>
<td>I have been so unhappy that I have had difficulty sleeping.</td>
<td>Yes, most of the time</td>
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<td>Yes, sometimes</td>
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<td></td>
<td>Not very often</td>
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<td></td>
<td>No, not at all</td>
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<td>8</td>
<td>I have felt sad or miserable.</td>
<td>Yes, most of the time</td>
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<td>Yes, quite often</td>
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<td>Not very often</td>
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<td></td>
<td>No, not at all</td>
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<td>9</td>
<td>I have been so unhappy that I have been crying.</td>
<td>Yes, most of the time</td>
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<td>Yes, quite often</td>
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<td></td>
<td>Only occasionally</td>
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<td></td>
<td>No, never</td>
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<td>10</td>
<td>The thought of harming myself has occurred to me.</td>
<td>Yes, quite often</td>
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<td>Yes, sometimes</td>
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<td></td>
<td>Hardly ever</td>
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<td>No, never</td>
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