

Anxiety among women experiencing medically complicated pregnancies: A narrative review of  
literature

by

Ambar Abrar  
MBA, IOBM-Pakistan, 2011

A Thesis Submitted in Partial Fulfillment of the  
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## Abstract

**Background:** Medical complications in pregnancy can be a significant source of stress for pregnant women and their partners. Despite this, and evidence that anxiety is very common among perinatal women, little is known about the relationship between perinatal anxiety and medical complications in pregnancy.

**Purpose:** The purpose of this research was to conduct a systematic review of the extant literature pertaining to medical complications of pregnancy and anxiety. Specific objectives were to (a) investigate differences in anxiety experience (symptoms and/or disorder) between women experiencing a medically complicated pregnancy and women experiencing a medically uncomplicated pregnancy, and (b) investigate the nature and scope of perinatal anxiety among women whose pregnancy is fraught with medical problems.

**Methods:** The review was guided by the PRISMA reporting process. The electronic databases MEDLINE and PsycINFO were searched to identify studies that met the study inclusion criteria. Data were extracted and presented in narrative form including tables and figures. An adapted form of the Newcastle-Ottawa Quality Assessment Scale for case-control and prevalence studies was used to perform a quality assessment review.

**Results:** Twelve studies met the inclusion criteria. Findings indicated that anxiety symptom severity was greater among women experiencing a medically complicated pregnancy compared to those experiencing an uncomplicated pregnancy. The prevalence studies in which symptoms of anxiety were assessed at various times during pregnancy, indicate that, among women experiencing a medically high-risk pregnancy, reported symptoms were most severe at initial assessment. Though, an exact estimate cannot be provided due to methodological differences, these studies reported the prevalence rates of anxiety symptoms to range from 7.8% to 46.9%. The

included studies that used DSM-IV criteria concluded that the risk may be most significant for two disorders: obsessive-compulsive disorder (OCD) and generalized anxiety disorder (GAD). Based on the overall quality of the available studies, the findings cannot be called as bias-free

**Conclusions:** Women experiencing a medically complicated pregnancy appear to experience significantly more symptoms of anxiety compared to women experiencing a healthy pregnancy.

## Table of Contents

Supervisory Committee.....	ii
Abstract.....	iii
Table of Contents.....	v
List of Tables.....	vii
List of Figures.....	viii
Chapter 1: Introduction.....	1
Chapter 2: Literature Review.....	4
Rationale for the Thesis Study.....	7
Research Questions.....	8
Chapter3: Methodology.....	9
Eligibility criteria.....	9
Databases.....	12
Literature search.....	13
Implementing the Search.....	16
Managing and Organizing Selected Literature.....	19
Data extraction tool.....	19
Risk of Bias/Quality Assessment.....	20
Narrative Synthesis of Results.....	22
Chapter 4: Results.....	25
Data Analysis.....	25
Group 1 (Case-Control Studies).....	26
Group 2 (Prevalence Studies).....	34
Descriptive analysis.....	38
Thematic Analysis.....	42
Risk of Bias/Quality Assessment.....	45
Chapter 5: Discussion.....	47
Conclusion.....	51
Implications for Clinical Practice.....	52
Suggestions for future researchers.....	52
Limitations.....	53
References.....	55

Appendix A.....	68
Newcastle-Ottawa Quality Assessment Scale.....	68
Appendix B.....	71
Newcastle-Ottawa Quality Assessment Scale.....	71
Appendix C.....	73
Quality Assessment.....	73

## List of Tables

Table 1: Study 1 Data .....	26
Table 2: Study 2 Data .....	27
Table 3: Study 3 Data .....	28
Table 4: Study 4 Data .....	29
Table 5: Study 5 Data .....	30
Table 6: Study 6 Data .....	31
Table 7: Study 7 Data .....	32
Table 8: Study 8 Data .....	33
Table 9: Study 9 Data .....	34
Table 10: Study 10 Data .....	35
Table 11: Study 11 Data .....	36
Table 12: Study 12 Data .....	37
Table 13: Summary Self-Report Anxiety Measurement Scores.....	41
Table A1: Quality Assessment Scale scoring table for case control studies .....	69
Table B1: Quality Assessment Scale scoring table for prevalence studies .....	72
Table C1: Study 1 quality assessment .....	73
Table C2: Study 2 quality assessment .....	73
Table C3: Study 3 quality assessment .....	74
Table C4: Study 4 quality assessment .....	75
Table C5: Study 5 quality assessment .....	75
Table C6: Study 6 quality assessment .....	76
Table C7: Study 8 quality assessment .....	77
Table C8: Study 12 quality assessment .....	78
Table C9: Study 9 quality assessment .....	79
Table C10: Study 10 quality assessment .....	79
Table C11: Study 11 quality assessment .....	80
Table.C12: Study 12 quality assessment.....	80

## List of Figures

Figure 1: The literature search process .....	14
Figure 2: PRISMA Flow Diagram .....	18

## **Chapter 1: Introduction**

Spielberger (2010), defines Anxiety as “an emotional state that includes feelings of apprehension, tension, nervousness, and worry accompanied by physiological arousal” in his book *State-Trait Anxiety Inventory* (p. 1). Anxiety is generally considered a normal response to life stressors, but it can become an issue when it is either too intense in relation to the stimuli, or occurs in response to non-threatening stimuli. Research shows that anxiety symptoms may remain unnoticed for long periods of time, and only become recognized when significant enough to interfere with functioning (Dokras et al., 2012). So, we can state that anxiety is a problem when it becomes overwhelming or unmanageable and it comes up unexpectedly. However, when anxiety lasts for weeks or months, develops into a constant sense of dread or begins to affect your everyday life, it may become an anxiety disorder. Anxiety disorders are mental illnesses that have a big impact on life.

Anxiety and related disorders are defined by DSM-5 (American Psychiatric Association, 2013), as “disorders that share features of excessive fear and anxiety and related behavioural disturbances” (p. 189). These disorders are characterized by a variety of psychological symptoms such as persistent fear, recurrent intrusive thoughts or concerns, feelings of tension, and avoidance behaviour. Physical manifestations of anxiety include signs of tachycardia, headache, sweating, tremors or hypertension. Resultingly, anxiety and related disorders impede psychosocial or physiological functioning and make individuals feel helpless (Marks & Lader, 1973).

Women are at a greater risk of developing anxiety and related disorders, and mood disorder, than men (Wenzel, 2011). Pregnancy and the postpartum period is a time when anxiety symptoms are common (Ross, & McLean, 2006; Wynter, Rowe, & Fisher, 2013). Perinatal anxiety is defined by some authors as the anxiety experienced by women during pregnancy and the

postpartum period (the first 12 months after birth) (Leach, Poyser, & Fairweather-Schmidt, 2017). Previously, perinatal mental health researchers focused mainly on women's experience of depression, but Ross and McLean (2006); Wynter, Rowe, and Fisher (2013), and Fairbrother and colleagues (2016) have shown that high levels of anxiety symptoms and anxiety disorders are typical at this time. Leach and colleagues (2017), in a recent systemic review of the literature, have demonstrated that both poor maternal health and complications during pregnancy are associated with higher levels of anxiety during the perinatal period.

Prenatal, maternal anxiety regarding future events, though a normal emotion, can become overwhelming and interfere with functioning. Various diseases and medical conditions may convert an ordinary pregnancy experience into high-stress situations for the mother, with negative clinical implications for the developing foetus. For example, diseases like preeclampsia and gestational diabetes have a strong association with high maternal morbidity, hospitalization, birth complications, and neonatal mortality (Hedderson, Ferrara, & Sacks, 2003; Martin Jr et al., 2012). Furthermore, the outcomes of these medical complications may cause an added burden to pregnant women and their families (Bayrampour et al., 2016). Multiple studies have found that pregnant women who experience medical complications also report higher levels of anxiety, compared to pregnant women without any such complications (Barber & Starkey, 2015; King et al., 2010). Besides physical implications, the psychological dynamics related to the stresses of a medically complicated pregnancy may also change (Levy-Shiff, Lerman, Har-Even, & Hod, 2002). Hence, a complicated pregnancy can be a source of additional stress and anxiety for mothers (Besser, Priel, Flett, & Wiznitzer, 2007; Johnson & Slade, 2003). Medical care for a complicated pregnancy presents further risks for maternal mental health (Denis, Michaux, & Callahan, 2012).

As discussed above, a high prevalence of psychiatric disorders during pregnancy, the added risk with medical complications, and a clear need for research examining the relationship between perinatal psychological problems and complicated pregnancies is the motivation for conducting a study in this area. The purpose of this study is to investigate what is known about symptoms of anxiety and the anxiety and their related disorders among women experiencing a medically high-risk pregnancy, so that mental health needs of these women can be projected in order to correctly allocate resources.

This review is guided by two objectives in reviewing the literature on perinatal anxiety in women with complicated pregnancies. First, the review tends to identify research on the level of anxiety symptoms, and the prevalence/incidence of anxiety and related disorders, among women experiencing medically complicated pregnancies compared with pregnant women, experiencing uncomplicated pregnancies, both in Canada and internationally. Second, the study seeks to identify, describe and evaluate the scope and nature of anxiety and stress in women who experience a medically complicated pregnancy. This work is an effort to provide information regarding the extent of the mental health needs of women with medically complicated pregnancies, to help guide the implementation of screening initiatives and clinical interventions for this group of women. Such information will be valuable for improving the health of pregnant women. It will also benefit their infants and families. This study represents is a narrative review of the research literature on anxiety and related disorders, and (self-reported) anxiety symptoms among women experiencing medically complicated pregnancies.

## Chapter 2: Literature Review

Anxiety and the related disorders, taken together, disproportionately affect women. These are the most common of all psychiatric conditions. The overall prevalence of these diseases is shown to be more than twice that of major depression; 18.1% versus 9.5% (Kessler et al., 2005). According to Kessler, Mickelson, and Williams (2009), about a quarter (28.8%) of all Canadians will suffer from an anxiety disorder in their lifetime. Furthermore, with an odds ratio (OR) of 1.6, the probability of occurrence of one these disorders among Canadian women is higher in comparison to men (Fairbrother, Young, Zhang, Janssen, & Antony, 2017). Anxiety and related disorders are associated with emotional and physical impairment and pose a significant economic burden for health care services (Koerner et al., 2004).

There are few published studies on the prevalence and incidence of anxiety and their related disorders, among women experiencing pregnancies affected by medical risk. However, the available research shows a high prevalence of these disorders (Barber & Starkey, 2015; Denis, Michaux, & Callahan, 2012; King et al., 2010). A medically high-risk pregnancy is defined by Gray (2006) as “any pregnancy in which there is evidence of the actual or potential threat of harm to the life or health of the mother and/or the baby, because of a disorder or situation coincidental with or unique to pregnancy” (p.217). According to Fairbrother and colleagues (2016), a medically complicated pregnancy has an increased risk of maternal and/or fetal complications, compared to a typical, healthy pregnancy. Health conditions that lead to increased risk can be obstetrical, maternal and/or fetal (Stahl, & Hundley, 2003). While a typical pregnancy resulting in a healthy birth can be a joyful experience for mothers and their families, about 15% of pregnancies have maternal/fetal medical complications (Alder, Fink, Bitzer, Hösli, & Holzgreve, 2007; Dagklis et al., 2016). These complications can invoke stressful emotional responses in parents which differ

from the usual stresses associated with parenthood (Jacob & Storch, 2013). For example researchers like Orr, Reiter, Blazer, and James (2007) have found a considerable variation in emotional responses in pregnant women with medically complicated pregnancies, which cannot be explained by generalized anxiety alone or even comorbidity with depression.

Anxiety symptoms have been found to be highly prevalent during pregnancy and puerperium (Fairbrother et al., 2015; Wenzel, 2011). Several researchers have explored the course of anxiety symptoms across the perinatal period (Dennis et al., 2013; Figueiredo & Conde, 2011; Paul et al., 2013). An increase in the symptomology is reported by Figueiredo and Conde (2011), in their study of Portuguese couples (N=560) throughout pregnancy. They reported an anxiety prevalence of 13.1% in the first trimester; 12.2% in the second trimester, and 18.2% in the third trimester. Researchers are also showing interest in investigating specific anxiety disorders during the perinatal period, including generalized anxiety disorder, panic disorder, post-traumatic stress disorder, obsessive-compulsive disorder, specific phobias related to pregnancy and childbirth, agoraphobia; social anxiety, and other anxiety disorders (Leach et al., 2017).

As described by Levy-Shiff, Lerman, Har-Even, and Hod (2002), a high-risk pregnancy is “any pregnancy in which a medical factor—maternal or fetal—may adversely affect the outcome of pregnancy, includes a wide array of conditions: maternal pre-pregnancy medical complications, pregnancy-induced medical complications, as well as fetal and labor complications” (p. 93). In a recently published study, Fairbrother and colleagues (2017) found a 5.17 times higher incidence of anxiety disorders among women experiencing a medically high-risk pregnancy, compared with women having a medically low-risk pregnancy. Professional organizations like the National Institute for Health and Care Excellence (Howard, Megnin-Viggars, Symington, & Pilling, 2014) and American College of Obstetricians and Gynaecologists (Lancaster et al., 2010) recognize the

risk of psychiatric illness in pregnancy and the postnatal period, including anxiety and related disorders. They recommend screening for mental health problems during this time.

Bayrampour and colleagues (2016) have argued that anxiety (even in the context of a healthy pregnancy) cannot be fully captured by current definitions of anxiety disorders. They suggest that it should be considered a discrete mental health entity. Furthermore, the added burden of uncertainty and high levels of stress in a high-risk and medically complicated pregnancy is shown to exacerbate the anxiety symptoms (Barber, & Starkey, 2015; Stainton et al., 2006). Researchers such as Cumberbatch, Birndorf and Dresner (2005), have shown that depressive symptoms and anxiety symptoms can be intensified during such pregnancies.

Medical complications impact not only the health and well-being of the mother but also her developing infant (and the entire family). Some early research (Hatmaker & Kemp, 1998) has demonstrated that 20% of expectant families are affected by these complications each year. Recent statistics (for the year 2016), have shown an estimated number of 800,000 complicated pregnancies in the United States, out of 4,000,000 total pregnancies (CDC/National Center for Health Statistics, 2016), and approximately 78,000 complicated pregnancies in Canada out of 400,000 pregnancies in total (CANSIM, 2016). Similarly, Fairbrother and colleagues (2017) have presented some statistics for the province of British Columbia: a prevalence of over 20% pregnancies with an obstetrical risk; accounting for up to 8000 births per year.

Medically complicated pregnancies lead not only to high maternal morbidity and mortality (as described earlier) but also contribute to a high-risk birth. An infant with a higher than average chance of mortality or morbidity in the first month of life is considered a high-risk infant (Fifer, Fingers, Youngman, Gomez-Gribben, & Myers, 2009). These preterm infants may suffer from complications such as neurological disorders, bronchopulmonary dysplasia, gastrointestinal

conditions or congenital malformations. In many cases, they need intensive medical care. Queenan, Hobbins, and Spong (2010) describe in “Protocols for high-risk pregnancies: an evidence-based approach,” preterm births give rise to very high financial costs for the public health system as well as the parents. The emotional damage due to a dysfunctional family system is also an important consideration (Allison, Wenzel, Kleiman, & Sarwer, 2011).

The overall management of medically complicated pregnancies (including hospitalization and bedrest) results in higher levels of distress and anxiety for affected women and their families. Maloni and colleagues (2006) have presented a positive association of hospital admission and bed rest with maternal stress levels. Separation from the family, lack of control, worry about the fetus, uncertainty and disrupted relationships may lead to higher distress and elevated anxiety levels in hospitalized women (Stainton et al., 2006). Additionally, the stress of complicated pregnancy may alter the coping skills of these women, and they may experience marital and family relationship difficulties (Sittner, DeFrain, & Hudson, 2005). All this evidence proves that anxiety in medically complicated pregnancies is an important area which merits a systematic review of the literature and future researchers’ attention.

### **Rationale for the Thesis Study**

The literature reviewed above shows that there is growing, albeit still limited, research investigating women with medically complicated pregnancies who suffer from anxiety disorders. Moreover, such diseases have an essential and deleterious impact on the health of the mother, the fetus as well as the mother’s partner and the family. With the emergence of new research, there is a need to summarize this literature. This may help to clarify relevant health-related variables associated with anxiety (and related disorders), especially in the context of complicated pregnancies (Armstrong, Hall, Doyle, & Waters, 2011). This study aims to target literature in two

areas: the presentation of (self-reported) anxiety symptoms or a diagnosis of anxiety (and related disorders) during a medically complicated pregnancy and the presence of gaps and uncertainties in the research. Resultantly, the researcher will be able to suggest areas where future research activity is needed. To conclude, this study will improve the understanding of anxiety and related disorders, and the presence of anxiety symptoms, along with their association to the medically complicated pregnancies.

### **Research Questions**

This review seeks the answers to the following three research questions:

1. Do women experiencing a medically complicated pregnancy experience higher levels of anxiety symptoms and/or a greater likelihood of a diagnosis of an anxiety or related disorder, compared with women experiencing a medically uncomplicated pregnancy?
2. What is known about the magnitude of the difference in levels of anxiety symptoms and/or anxiety and related disorder prevalence between women experiencing a medically complicated pregnancy and women experiencing a medically uncomplicated pregnancy?
3. What is known about the nature and scope of: (a) symptoms of anxiety and (b) the prevalence of the anxiety and related disorders, among women experiencing a medically complicated pregnancy?

### **Chapter3: Methodology**

This study is a narrative literature review of the relevant research. A literature review is a comprehensive summary of evidence from multiple studies (Shea et al., 2007). The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Shamseer et al., 2015) were followed to bring together available evidence in this area of interest. PRISMA is the most commonly used reporting system for systematic reviews and meta-analyses. It is a reliable and practical instrument being used by systematic reviewers since 1999 to ensure consistent results. This statement guides researchers to comprehensive reporting of methods and conclusions of included studies so that an adequate critical appraisal can be provided. The PRISMA statement consists of a checklist of items to be included in each section of the systematic review: title, abstract, introduction, methods, results, discussion, and funding which guides authors to perform a verification of the items that compose it. Moreover, this statement is easy to use, and a flow diagram helps the researcher in this process.

The review was conducted using specific eligibility criteria to determine which studies to include in the review. The following list details those inclusion and exclusion criteria.

#### **Eligibility criteria**

For this review we employed the following inclusion and exclusion criteria:

#### ***Inclusion***

- 1) Participants in the individual studies were required to be either:
  - (a) adult pregnant women experiencing a medically complicated pregnancy only, or
  - (b) adult pregnant women experiencing a medically complicated pregnancy and adult pregnant women experiencing a medically uncomplicated pregnancy.
- 2) Outcome variables: An assessment of the following was required for study inclusion:

- (a) anxiety disorders (i.e., one of eight common anxiety disorders which include Panic Disorder, Agoraphobia, Obsessive-Compulsive Disorder, Generalized Anxiety Disorder, Social Phobia, Specific Phobia, Posttraumatic Stress Disorder, and Anxiety Not Otherwise Specified) confirmed by a diagnostic interview, or
  - (b) symptoms of anxiety assessed by a psychometrically validated questionnaire.
- 3) Research design: Observational (cross-sectional, case-control and cohort).
  - 4) Timeframe: The review required the studies to be published in last twenty-three years (1994-2017).
  - 5) Other: The review was limited to peer-reviewed articles in the English language, and research involving human participants only.

### ***Exclusion***

Studies were excluded from the review for the following reasons:

- 1) failure to use a validated questionnaire, or a structured diagnostic interview according to DSM criteria; or
- 2) if the study methodology was limited to any of the following:
  - (a) retrospective studies or chart reviews;
  - (b) postpartum studies;
  - (c) qualitative studies/case reports/case series;
  - (d) articles covering only high-risk pregnancy, without relating it to the aspects of mental distress or anxiety disorders;
  - (e) studies of anxiety and related disorders alone; and
  - (f) book chapters.

### ***Rationale for inclusion and exclusion***

This inclusion/exclusion criteria of this review allowed the selection of the most relevant studies to answer the stated research questions: (a) to assess whether there exists a difference in anxiety symptoms/disorders among women experiencing a medically complex pregnancy and those experiencing a medically uncomplicated pregnancy, (b) the magnitude of the difference, and (c) the nature and scope of (a) symptoms of anxiety and (b) the prevalence of the anxiety among women experiencing a medically complex pregnancy.

I selected studies in which either anxiety disorders or symptoms of anxiety were assessed categorically as a mental health disorder or dimensionally as an emotional state or collection of symptoms. To ensure the reliability and validity of the measure, I chose to include only those studies in which anxiety disorders were assessed via diagnostic interview (the gold standard for anxiety disorder assessment) or those in which anxiety symptoms were assessed with psychometrically sound instruments.

The first two research questions pertain to potential differences which may exist between women experiencing a medically complicated pregnancy and healthy women so. Given that this research question involves comparisons between two groups, and no variables are manipulated, a case-control methodology is the appropriate design. The third question can be answered using any of the following research designs: case-control, cohort or cross-sectional. Consequently, only studies using these study designs were eligible for inclusion. I excluded experimental studies, chart reviews, case reports, book chapters and retrospective studies because they were not suitable to answer the research questions. I included the studies which measure both the variables to find out the association between disease (anxiety) and risk factors (medical complications), therefore, anxiety only and medical complication only studies were excluded. Postpartum studies were

excluded because a measurement of anxiety symptoms during the course of a complicated pregnancy was required.

I included only studies conducted from year 1994 onwards to conform to the reference standards of Diagnostic and Statistical Manual of Mental Disorders DSM-IV (American Psychiatric Association, 1994) or later criteria for the diagnosis of anxiety disorders or anxiety symptoms. This time frame also allows studies using DSM-5 (American Psychiatric Association, 2013) diagnostic criteria. The DSM is the handbook used by clinical psychiatrists in North America and much of the world. It is considered an authoritative guide to the diagnosis of psychiatric disorders. To conform to the research standards and complete understanding, I allowed only peer-reviewed English language studies.

## **Databases**

A database is a searchable collection of information consulted for the specific purpose of the research. Researchers choose databases for literature search, keeping their relevance to the research area in view. For the current review, a comprehensive search was carried out in two major databases cataloguing biomedical information. MEDLINE (citations and abstracts in medicine, public health, nursing, dentistry, veterinary medicine, and the preclinical sciences), and PsycINFO (database of psychological literature sponsored by the American Psychological Association) is the repository of articles published in medical and health journals. To ensure a targeted search, various databases storing mental health research journals were tested. MEDLINE and PsycINFO produced the most extensive coverage of literature on our topic area. Additionally, the references found in both of the databases were significantly more accessible.

## **Literature search**

### ***Strategy***

A combination of MeSH, keywords, and subject headings (in text and titles) were used for literature search from each database (Figure 1).

*Keywords:* The search used natural language words for describing a topic in both of the databases.

*Subject headings:* Pre-defined words were used to describe the contents of each journal article in the database of PsycINFO.

*MeSH:* Medical Subject Headings; the US National Library of Medicine guided vocabulary thesaurus for indexing articles, were used in the databases of PubMed.

### ***Methods***

Database searches were conducted for anxiety symptoms in pregnant women for various high-risk medical conditions using MeSH terms, subject headings or keywords (listed as search terms). These keywords and phrases were developed from the research questions. This process helped to identify the amount of literature available for each state, and the degree of overlap in the literature across these conditions. Later, these search terms were combined by using the Boolean operators to get a comprehensive research overview. The Boolean operators (AND, OR, NOT or AND NOT) were used as conjunctions to produce focused and productive results. These operators save time by concentrating searches for more 'on-target' results (Frants, Shapiro, Taksa, & Voiskunskii, 1999).

*Electronic search:* The PRISMA statement recommends to present a detailed search strategy ((Liberati et al., 2009) therefore (guided by Figure 1), for the databases of MEDLINE and PsycINFO :

- The search terms were identified by breaking down the research question for critical concepts such as anxiety, pregnancy, complications, and medical disorders.
- Each key term was entered into the database thesaurus and “suggest subject terms” option was selected. A list of controlled word-stock was generated for all the keywords. Their related terms were also checked, (when necessary) so that the different aspects of a main concept could also be searched for.

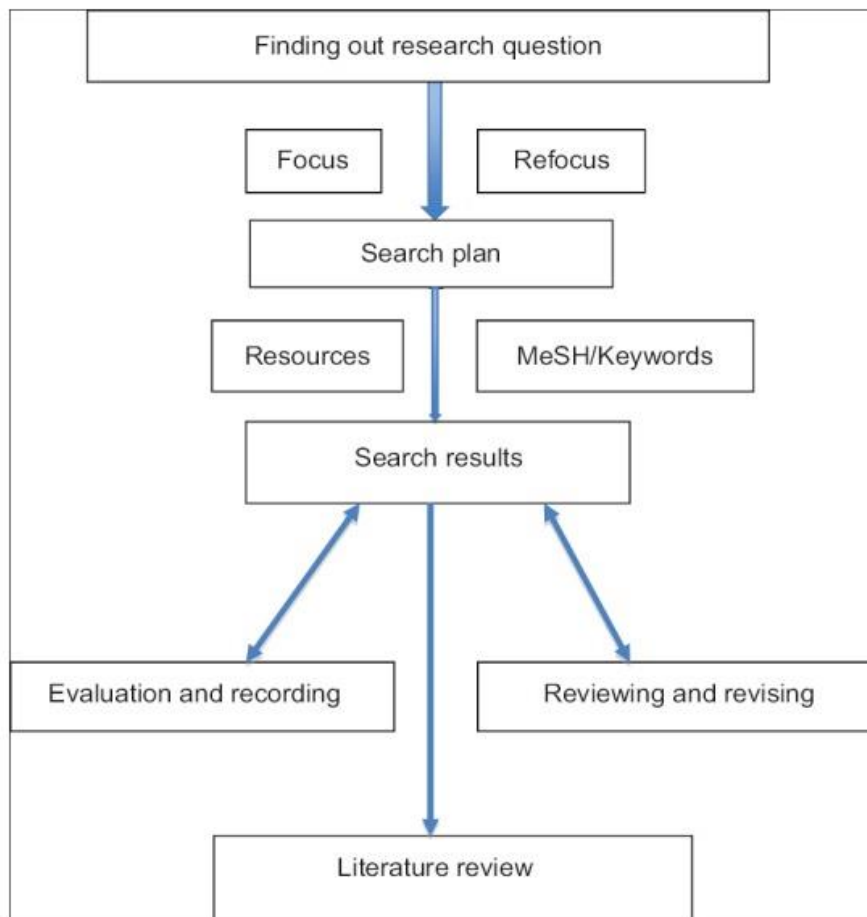


Figure 1: The literature search process (adapted from Grewal, Kataria, & Dhawan, 2016).

- The definitions of all suggested terms were read, and where the definition matched the understanding of the concept under search, the desired terms was selected.

- The preferred terms were exploded (to include all the narrower terms associated with the broad concept) for eliciting further information. The results showed all the studies using the selected words.
- The search results for all the main concepts were joined using boolean operators “AND” and “OR”.
- The search was further narrowed down through the advanced search option; selecting the specific “age group”, and “population group”. Moreover, date and publication restriction also helped in getting the targeted results.
- The final list of focused results was extracted for abstract review.

### *Search terms*

For this SLR, a set of search terms, selected after consultation with the research supervisor (regarding specific concepts within the research questions) and the subject librarian (for database-controlled vocabulary) included:

(“pregnancy” OR “pregnant women”) AND (“anxiety” OR “anxiety symptoms” OR “anxiety disorders” OR “Panic Disorder” OR “Obsessive Compulsive Disorder” OR “phobias” OR “Posttraumatic Stress Disorder”) AND (“Pregnancy, high-risk” OR “Pregnancy complications” OR “Hypertension” OR “Hypertension pregnancy-induced” “Pre-eclampsia” OR “Diabetes Mellitus” OR “Diabetes Gestational”)

Refinements of the MeSH/key terms has been done with assistance from Rebecca Raworth (Island Medical Program Librarian, Learning & Research Librarian) Health Information Science & Neuroscience – McPherson Library University of Victoria.

*Manual search:* The reference lists/ bibliography of the retrieved articles were also searched manually to find further related publications. Relevant grey literature repositories were

also explored (to collect data from protocols and program documents), when available. Hand-searched materials were saved as additional records.

### **Implementing the Search**

Finally, a thorough systemic search was done to find the desired research articles and each step was recorded. Different combinations of key terms, (selected from the relevant databases as described earlier) were entered in the database in the following order:

- 1) Login to University of Victoria library page.
- 2) Select EBSCO-MEDLINE database.
- 3) Go to Advance Search option.
- 4) Select subject terms:
  - a) Search 1: (“anxiety” OR “anxiety symptoms” OR “anxiety disorders” OR “Panic Disorder” OR “Obsessive Compulsive Disorder” OR “phobias” OR “Posttraumatic Stress Disorder”)
  - b) Search2: (“Pregnancy” OR “Pregnant women”)
  - c) Search 3: (“Hypertension” OR “Hypertension pregnancy-induced” OR “Pre-eclampsia”)
  - d) Search 4: (“Diabetes Mellitus” OR “Diabetes Gestational)
  - e) Search 5: (“Pregnancy, high-risk”)
  - f) Search 6: S2 AND S3
  - g) Search 7: S2 AND S4
  - h) Search 8: S6 OR S7OR S5
  - i) Search 9: S8 AND S1
  - j) Search 11: S10 with Limiter (English language)

- k) Search 12: S10 with Limiter (Date of publication)
- l) Search 13: S10 with Limiter (Subject age)
- 5) The search results were filtered using inclusion/exclusion criteria to eliminate irrelevant or redundant articles.
- 6) The studies found from other sources were included in the study list.
- 7) All the titles and abstracts thus extracted were read, and the duplicates and non-relevant references were removed.
- 8) From the finalized list, full studies meeting all the inclusion criteria were reviewed.
- 9) The studies not answering the research questions were removed.
- 10) The relevant studies were carefully read by myself and a student volunteer to confirm the final selection according to the inclusion-exclusion criteria.
- 11) Uncertainty was resolved by supervisory team consensus.

A modified PRISMA Flow diagram (Figure 2) summarizes this study selection process.

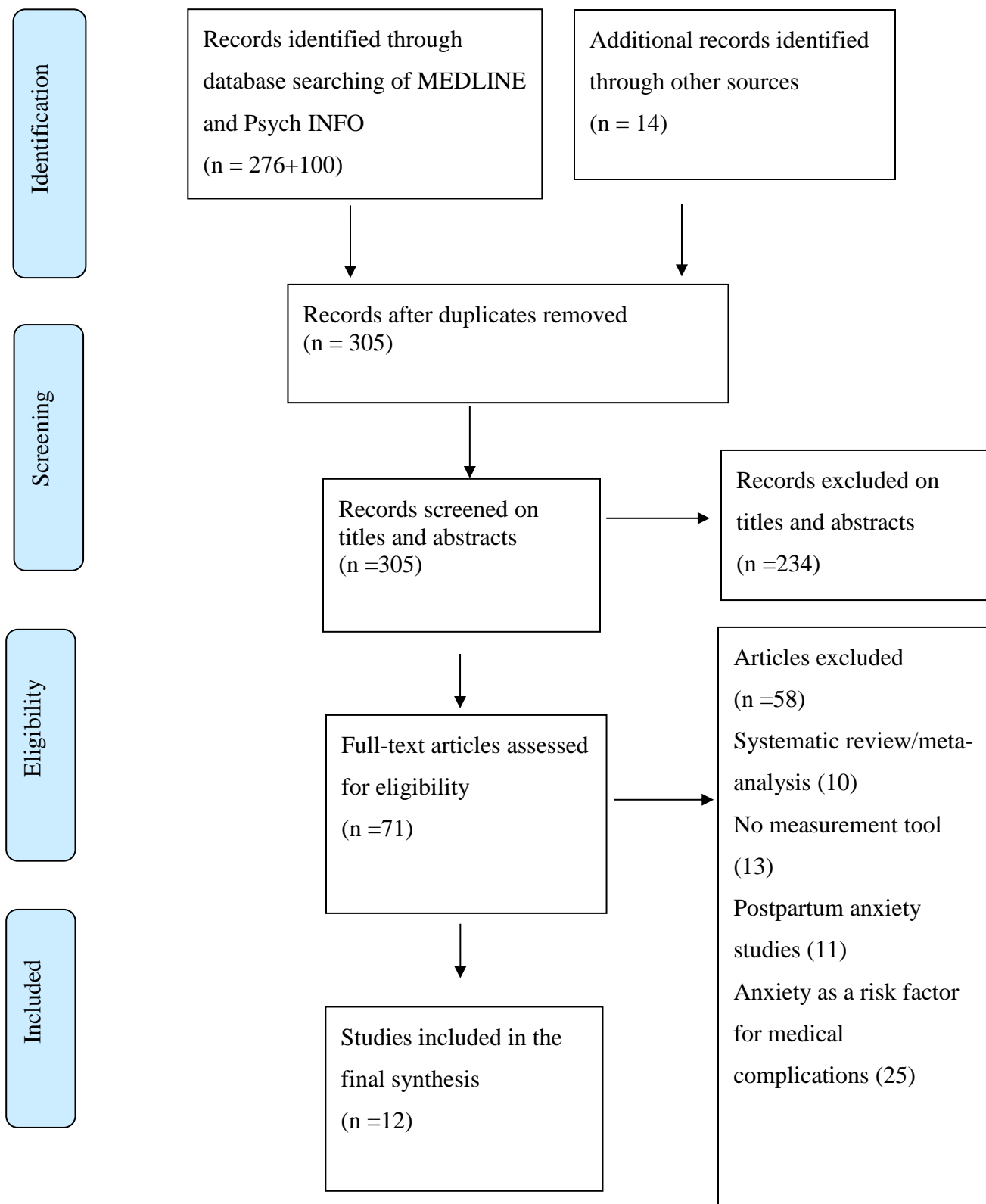


Figure 2: PRISMA Flow Diagram (adapted from Shamseer et al., 2015)

## **Managing and Organizing Selected Literature**

Mendeley; the reference manager and the academic network, was used to help organize this research study. The reference management programs organizes the selected research studies, identifies and eliminates duplicate records, and helps in the accurate reference citing (Lorenzetti & Ghali, 2013). Ideally, studies should be collected independently by a team of researchers and checked by the lead author after entry into the software. However, for this thesis, I collected the articles and extracted the required information using the pre-described data extraction technique, and a student volunteer checked the collection process.

### **Data extraction tool**

The Cochrane Handbook for Systematic Reviews of Interventions (Higgins & Green, 2008) proposes some essential “characteristics of studies” for data extraction. Based on these recommendations, the extracted data from the studies include:

#### ***Study ID***

- The first author (first and last name)
- Year of publication

#### ***Methods***

- The study design;
- The sample size/sizes;
- The definition of cases and controls

#### ***Characteristics of the study participants***

- Mean gestational age of the women at anxiety assessment;
- The country where the study was conducted;
- The study settings

- The high-risk condition;

### ***Measures***

- Tool for anxiety assessment;
- The assessment timing;

### ***Outcomes***

- Anxiety diagnosis or anxiety scale scores
- Conclusions

### **Risk of Bias/Quality Assessment**

The PRISMA guidelines recommend describing the methods used to gauge the risk of bias in the included studies and also elaborate how this information can be used by the authors (Shamseer et al., 2015). The risk of bias assessment of individual studies is part of evaluating the strength of a body of evidence. It is mostly carried out in randomized controlled trials. Each RCT study is evaluated for precision, directness, and applicability of the evidence. According to the Cochrane Handbook for Systematic Reviews of Interventions, the risk of bias, is defined as “a systematic error or deviation from the truth, in results or inferences” (Higgins & Green, 2008, p. 20). It is important to mention that the strength of evidence is independent of the magnitude of impact reported in a research paper. We may get a substantial evidence in favour of a small effect size or weak evidence about ostensible findings (Lohr, 2004).

For non-randomized studies, many authors provide this assessment by describing the “quality” of the research study (Jahan, Naveed, Zeshan, & Tahir, 2016). In “Systematic reviews in the social sciences: A practical guide”, Petticrew (2006) also describes quality assessment requirements for various types of non-randomized observational studies. Lohr (2004) has defined quality assessment as “the extent to which all aspects of a study’s design and conduct can be shown

to protect against systematic bias, nonsystematic bias, and inferential error” (p. 472). Studies with cohort and case-control designs, pose an additional challenge to implement and conduct (Viswanathan et al., 2008). Biases can be found in subject selection, measuring outcomes, and differences in the study groups (cases and controls); which may influence the study results. Therefore, the quality assessment of such studies is essential for understanding the extent to which the design, conduct, and analysis of a study have minimized biases. This quality assessment is provided by multiple researchers separately, using pre-defined criteria. However, at present, there is no consensus among the researchers on the best approach or preferred tool for quality assessment. As the components associated with risk of bias are in contention, there is no universal tool that addresses all the varied contexts to assess the study quality assessment. Though some standardized instruments are widely used by research reviewers to evaluate various study designs (Viswanathan et al., 2008).

Keeping above mentioned factors in view, the Newcastle-Ottawa Scale (NOS) was selected for quality assessment of the studies included in this review (Wells et al., 2009). The NOS is a validated instrument specifically developed to assess the quality of design and content of non-randomized studies. Researchers have widely used it as a reliable tool for quality assessment, as described by Lo, Mertz and Loeb (2014). Two adapted versions of this instrument were used for this review, to evaluate case-control and cohort studies. The original scale evaluated the studies on three generic parameters: the study groups’ selection; the study design, and the data collection. A star system was used to rate each item in these three sections. We used four criteria to appraise each study: (1) the appropriateness of the study design to answering the review question, (2) the presence of potential selection bias, (3) the validity of data collection methods, and (4) the appropriateness of data analysis to the research question. We also changed the ranking system to

a points based method, for ease of score calculation. Each item was awarded a number from 0-2, with “a” representing the highest quality (i.e., a 2), and “c” representing the lowest (i.e., a 0). Based on the total score, each study was rated as STRONG, MODERATE or WEAK. (Appendix B). This quality assessment was used by myself and a student volunteer separately. Later our individual results were matched, and a final rating was issued by mutual consensus.

### **Narrative Synthesis of Results**

The process of bringing the findings from a set of studies together, so that a conclusion can be drawn, is called a result synthesis. Based on the body of evidence, two main approaches to synthesis development include quantitative and narrative synthesis. ‘Narrative’ synthesis’, according to Popay and colleagues (2006), is “an approach to the systematic review and synthesis of findings from multiple studies that rely primarily on the use of words and text to summarize and explain the findings of the synthesis” (p. 5). This method is frequently used for evidence synthesis in systematic reviews. Narrative synthesis is employed to answer a wide range of questions across disciplines, including clinical research. The colorectal cancer study by Eisen and Weinberg (2005), is one example. Some steps from the process, as described by the Guidance on the Conduct of Narrative Synthesis in Systematic Reviews (Popay et al., 2006), include:

#### ***Preliminary descriptions***

A descriptive paragraph on every single included study was produced as a starting point in an initial synthesis. This step is useful for the recording purpose.

#### ***Groupings and clusters***

This process involved organizing the studies into smaller groups. Done at any at an early stage, this made the review process more manageable. However, it became necessary to refine these groups as the synthesis evolved.

### ***Tabulation***

The visual representation of both quantitative and qualitative data is a common approach employed in all types of systematic reviews (Evans, 2002). Tabulation was useful in developing an initial description of the included studies; identifying patterns across studies and providing building blocks for elements of the synthesis process. A tabulation also proved to be a valuable tool in the results formulation.

### ***Descriptive data analysis***

Unlike a meta-analysis, the study results were not pooled statistically, but rather in a narrative synthesis; the process was unable to produce a single estimate of effect size (Shadish, 1996). However, transforming study results into a common rubric allowed the reviewers to develop a meaningful summary of study results. Therefore, a descriptive method of vote-counting was used to calculate the frequency of different types of results across included studies. Some researchers have favoured vote-counting as an intrinsic element of any narrative synthesis (Cwikel, Behar, & Rabson-Hare, 2000). They found this type of analysis to be a useful way of producing a description of patterns across the included articles.

### ***Thematic data analysis***

Several researchers favour thematic analysis for organizing and summarizing the findings from diverse bodies of research such as health sciences (Mays, Pope, & Popay, 2005; Stemler, 2001). Thematic analysis for this thesis was developed inductively; there were no prior themes to guide data analysis from the outset of this review. Such an analysis helped capture the main concepts and conclusions across studies, rather than producing new knowledge. The primary reported themes were used to explore the similarities and differences between the included studies.

### ***Exploring the relationships between studies***

Multiple conceptual models were used to explore the relationships within and across the included studies. These approaches employed grouping of the findings together, which reviewers considered conceptually similar. Later, the relationships between these groupings were also identified.

### ***Validity assessment***

Assessing the strength of evidence, extracted from the included studies, is a part of the narrative synthesis. Researchers for this review used specific tools to define “weak”, “moderate” or “good” evidence, explicitly.

### ***Conclusion***

In the case of narrative synthesis, the product of the systematic review may not be able to provide a ‘meta-answer’ to the primary research question. None the less, a theoretical understanding of the underlying mechanisms of the results was presented.

## **Chapter 4: Results**

The review used a narrative synthesis to analyze the included articles; the data was gathered using the above-mentioned data extraction tool. Findings were systematically organized and tabulated for all the included studies. Subsequently, the results were presented applying a narrative summary of the findings of the quantitative outcome evaluations, as recommended by systemic review guidelines (Petticrew & Roberts, 2006).

### **Data Analysis**

Following the narrative result synthesis guideline (described in the methodology section), the selected studies were organized into two groups, according to the research questions they are designed and able to answer. Group one included only those studies in which a case-control design was employed (See Tables 1 to 8). Group two included longitudinal prevalence studies (See Tables 9 to 12) which studied women longitudinally over the perinatal period. They were arranged separately as only a proportion of the included studies were relevant and informative to my first two research questions, whereas all of the included studies spoke to my third research question. The data from these studies were extracted using the data extraction tool (pre-defined) and tabulated for result synthesis.

## Group 1 (Case-Control Studies)

Table 1: Study 1 Data

Study ID / Country	Study design	Sample size	Assessment timings	Study settings	Medical condition	Tool for anxiety assessment	Anxiety scale scores	Conclusions
Fairbrother et al. (2016)  Canada	Prospective cohort / case-control	N=310  Low-risk (n = 169) Moderate-risk (n = 76) High-risk (n = 65)	13 weeks postpartum	BC Women's Hospital	Maternal /fetal High-risk, based on Perinatal Services BC Maternal and Fetal Levels of Service Classification Tool	Structured Clinical Interview for DSM-IV	The relative risk of an anxiety disorder was found to be 6.58 times greater for women with a medically moderate risk pregnancy and 5.17 times higher for medically high-risk pregnancy (95% CI) compared to the low-risk women. The highest probability was for GAD and OCD	Women experiencing pregnancies with medical issues affecting either the mother or the developing infant appear to be at elevated risk for the development of AD. But, across risk groups, there were no differences in AD prevalence or in the incidence of AD in the postpartum.
Controls (Low-risk): Maternal and/or fetal concerns not anticipated to impact well being		Cases (Moderate-risk): Maternal and/or fetal concerns that could potentially impact well-being			Cases (High-risk): Maternal and/or fetal concerns that most likely impact well-being and may be life-threatening			

Table 2: Study 2 Data

Study ID / Country	Study design	Sample size	Assessment timings	Study settings	Medical condition	Tool for anxiety assessment	Anxiety scale scores	Conclusions
Uguz et al. (2012) Turkey	Case-control study	N=142 (n1=52) (n2=90)	The first trimester of the gestation	Research and Training Hospital of Konya University Turkey	Hyperemesis gravidarum (HG)	1) Structured Clinical Interview for DSM-IV  2) Structured Clinical Interview for DSM, (III-R) Personality Disorders (SCID-II)	The prevalence of any anxiety disorder in women with HG was 36.5%,  36.5% of the patients with HG had at least one personality disorder  GAD had the highest prevalence	The prevalence of major depression, generalized anxiety disorder, avoidant personality disorder and obsessive-compulsive personality disorder was significantly higher in women with HG compared to the control subjects.
Cases: Pregnant women with Hyperemesis gravidarum (HG)					Control: Healthy pregnant women			

Table 3: Study 3 Data

Study ID / Country	Study design	Sample size	Assessment timings	Study settings	Medical condition	Tool for anxiety assessment	Anxiety scale scores	Conclusions
Gupton et al. (2000) Canada	Case-control study	(N=208) (n1=105) (n2=103)	Gestational age 27 to 36 weeks	Two major teaching hospital Isofa city in western Canada	Women with complication of pregnancy, such as preeclampsia, antepartum haemorrhage, premature rupture of membranes, preterm labour, or gestational diabetes	Spielberger State Trait Anxiety Inventory (STAI) The Perception of Pregnancy Risk Questionnaire (PPRQ)	(STAI)Mean scores for Complicated pregnancies: 42.3 (12.7) Uncomplicated pregnancies: 34.4 (10.3) (PPRQ)Mean Scores for Complicated pregnancies: 474.3 (178.2) Uncomplicated pregnancies: 265.4 (148.6)	The state anxiety score was the second predictor of pregnancy risk score, after the biomedical risk score.
<i>Cases:</i> Women having a complicated pregnancy requiring hospitalization for more than 48 hours					<i>Controls:</i> Women with no known complications			

Table 4: Study 4 Data

Study ID / Country	Study design	Sample size	Assessment timings	Study settings	Medical condition	Tool for anxiety assessment	Anxiety scale scores	Conclusions
Marquesim et al. (2015) Brazil	Prospective Case-control study	(N=105) (n1=66) (n2=39)	Gestational age 27 to 36 Weeks  First prenatal visit or the time of disease diagnosis (T1)  Admission for delivery (T2)	A state university hospital in the southeastern part of Brazil	Diabetes Mellitus	State Trait Anxiety Inventory (STAI)	Women with hyperglycemia and normal glucose level showed similar levels of anxiety, but at (T1), severe state anxiety was more frequent in women with hyperglycemia compared to the control group (25.8% vs 7.7 %, p = 0.041)	The incidence of severe state anxiety in early pregnancy is more frequent in women with diabetes or hyperglycemia, but their levels of trait anxiety are not affected by glycemic status.

Cases:

Pre-pregnancy diabetes (DM), mild gestational hyperglycemia (MHG), and gestational diabetes (GDM)

Controls:

Women with normal glucose levels (NG group)

Table 5: Study 5 Data

Study ID / Country	Study design	Sample size	Assessment timings	Study settings	Medical condition	Tool for anxiety assessment	Anxiety scale scores	Conclusions
Bjørk et al. (2015) Norway	Prospective case-control study	N=706 (cases) N=106511(control)	From the second trimester to 36 months after delivery	Norwegian Mother and Child Cohort	Epilepsy	Hopkins Symptom Checklist (SCL)	Women with epilepsy more often had peripartum anxiety (22.4%) than women without epilepsy (14.8%) (p < 0.001)	Women with epilepsy frequently have anxiety during and after pregnancy.
Cases: Pregnant women with epilepsy					Controls: Community women			

Table 6: Study 6 Data

Study ID / Country	Study design	Sample size	Assessment timings	Study settings	Medical condition	Tool for anxiety assessment	Anxiety scale scores	Conclusions
Barber & Starkey (2015)  New Zealand	Case-control study	N = 232 (n1=118) (n2=114)	Pregnancy of at least eight weeks' gestation	In patient antenatal unit of Waikato Hospital and community-based settings in New Zealand	Pregnant women hospitalized for complications	State Trait Anxiety Inventory (STAI)	STAI Mean State Anxiety scores: Cases= 41.33 (12.12) Controls=37.48 (12.10)  STAI Mean Trait Anxiety scores: Cases=38.16 (9.43) Controls=37.61 (10.47)	Many women hospitalized during pregnancy are extremely anxious. The most vulnerable are those who are less optimistic and see their health as poor
Cases: Pregnant women hospitalized for complications					Controls: Community comparison group			

Table 7: Study 7 Data

Study ID / Country	Study design	Sample size	Assessment timings	Study settings	Medical condition	Tool for anxiety assessment	Anxiety scale scores	Conclusions
Cetin et al. (2016) Turkey	Case-control study	N = 152 (n1=45) (n2=41) (n3=44)	Postpartum period	Three large urban teaching hospitals in Philadelphia	Preeclampsia/ Gestational Hypertension	Hospital Anxiety and Depression Scale (HADS)	The severe preeclamptic had the highest scores on the HAD Scale (14.0±3.6), followed by the mild preeclamptic group (5.4±3.1), compared to the healthy women (1.0±1.8) (p: 0.001)	Preeclampsia negatively affects the psycho-emotional state, psychopathological symptoms and sleep patterns.
Cases: 1-Pregnant women with mild pre-eclampsia 2-Severe preeclamptic postpartum women.					Controls: 3-Healthy pregnant women			

Table 8: Study 8 Data

Study ID / Country	Study design	Sample size	Assessment timings	Study settings	Medical condition	Tool for anxiety assessment	Anxiety scale scores	Conclusions
Kender et al. (2016) Turkey	Case-control study	N= 92 (n1=51) (n2=41)	Within three days of giving birth	Okmeydani Research and Training Hospital Turkey	Hyperemesis gravidarum	Beck Anxiety Inventory	Anxiety levels were higher in the hyperemesis gravidarum group; 19.22 (10.96) compared to the control group; 11.71 (8.21).	Anxiety levels were higher in pregnant women diagnosed with hyperemesis gravidarum compared to healthy pregnant women.
Cases: Pregnant women with HG					Controls: Healthy pregnant women.			

## Group 2 (Prevalence Studies)

Table 9: Study 9 Data

Study ID / Country	Study design	Sample size	Assessment timings	Study settings	Medical condition	Tool for anxiety assessment	Anxiety scale scores	Conclusions
Gourounti et al. (2015) Greece	Prevalence study	N= 133	T1: Trimester 1 T2: Trimester 2 T3: Trimester 3	Two public hospitals in Athens	A history of previous complications in pregnancy or preexisting medical conditions or current 'high risk' pregnancy	State Trait Anxiety Inventory (STAI)	State anxiety, mean (SD): T1=46.3 (10.8), T2= 50.2 (10.2), T3=53.8 (14.8)  Trait anxiety, mean (SD): T1=47.8 (5.1), T2= 43.3 (7.7), T3= 45.2 (8.5)	A vast majority of these women experience antenatal Anxiety. The prevalence of antenatal anxiety identified in this study is of concern.

Cases:

High-risk pregnant women hospitalized in the inpatient antenatal ward

Table 10: Study 10 Data

Study ID / Country	Study design	Sample size	Assessment timings	Study settings	Medical condition	Tool for anxiety assessment	Anxiety scale scores	Conclusions
Peng Chiong Tan et al. (2016)  Malaysia	Prevalence study	N= 209	First Trimester	University of Malaya Medical Center	Hyperemesis gravidarum and hospitalization	Hospital Anxiety and Depression Scale (HAD)	46.9% of study participants fulfilled criterion for anxiety caseness.  The anxiety prevalence rate was 36.3% in healthy pregnant women was used for a comparison	Anxiety and depression caseness is common in HG and risk factors can be identified. There is no convincing association between anxiety and depression and more severe illness.

Cases:  
Pregnant women hospitalized for presumed HG

Table 11: Study 11 Data

Study ID / Country	Study design	Sample size	Assessment timings	Study settings	Medical condition	Tool for anxiety assessment	Anxiety scale scores	Conclusions
Byatt et al. (2014) USA	Prevalence study	N= 62	Initial Interview Seven days after admission, (up to 4) follow-up surveys on a weekly basis, and postpartum survey	An academic medical centre in Central Massachusetts	High-risk obstetrical complications	Generalized Anxiety Disorder (GAD-7)	The anxiety prevalence rate was 13% at initial survey. Mean anxiety initial and postpartum: 4.2±6.5 vs 5.2±5.1, (p=.011)	Hospitalized high-risk obstetrical patients may commonly experience depression symptoms and anxiety symptoms and not receive treatment.

Cases:

Women admitted to the antenatal service due to high-risk obstetrical complications

Table 12: Study 12 Data

Study ID / Country	Study design	Sample size	Assessment timings	Study settings	Medical condition	Tool for anxiety assessment	Anxiety scale scores	Conclusions
Jing Chen et al. (2016) China	Prevalence study	N= 197	T1: Baseline T2:6 Months T3:7Months T4:8 Months T5:9 Months	International Peace Maternity and Child Health Hospital, Shanghai	A history of previous complications in pregnancy or current 'high risk' pregnancy	Hospital Anxiety and Depression Scale (HAD)	Anxiety prevalence was 7.8% at T1.  Mean (sd) HAD anxiety score among 'high-risk' women were: T1=3.69 (2.76), T2= 3.28 (2.70) T3= 3.04 (2.73) T4= 3.04 (3.02) T5= 2.69 (2.77).	Anxiety and depression symptoms are commonly seen in pregnant women with a history of previous complications or current 'high risk' pregnancy

Cases: High risk' if they met any of the following criteria:

(a) having a history of complications: a history of stillbirth or fetal mortality, history of giving birth to a congenital abnormal fetus;

(b) test tube babies, pregnancy at a later age, scarred uterus

## **Descriptive analysis**

### ***Study characteristics***

The 12 studies were conducted across various countries including three in Turkey (Cetin et al., 2016; Kender et al., 2016; Uguz et al., 2012), two in Canada (Fairbrother et al., 2016; Gupton et al., 2000), one each in China (Jing Chen et al., 2016), Greece (Gourounti et al., 2015), Brazil (Marquesim et al., 2015), Norway (Bjørk et al., 2015), New Zealand (Barber & Starkey, 2015), Malaysia (Peng Chiong Tan et al., 2016), and the USA (Byatt et al., 2014). An interesting finding was that researchers from developing countries made a more significant contribution in perinatal mental health research compared to the developed nations. All the research was conducted in public hospitals/medical centres except the Norwegian Mother and Child Cohort study (Bjørk et al., 2015), in which the data were extracted from a population database.

The sample sizes in these studies ranged from 62 to 107217 women. Group one studies had a sample size range of 92 (Kender et al.) to 107217 (Bjørk et al., 2015) where as group two studies included 62 (Byatt et al., 2014) to 209 (Peng Chiong Tan et al., 2016) participants. The research designs of group one included: six case-control studies (Barber & Starkey, 2015; Cetin et al., 2016; Gupton et al., 2000; Kender et al., 2016; Marquesim et al., 2015; Uguz et al., 2012), one cohort study with a nested case-control design (Fairbrother et al.), and one case-control study based on a large sample drawn from a population cohort (Bjørk et al., 2015) Group two had four prevalence studies (Byatt et al., 2014; Gourounti et al., 2015; Jing Chen et al., 2016; Peng Chiong Tan et al., 2016).

### ***Measurement tools used and assessment time points***

Ten out of twelve reviewed studies (Barber & Starkey, 2015; Bjørk et al., 2015; Byatt et al., 2014; Cetin et al., 2016; Gourounti et al., 2015; Gupton et al., 2000; Jing Chen et al., 2016;

Kender et al., 2016; Marquesim et al., 2015; Peng Chiong Tan et al., 2016) used self report measures to compare anxiety in women with and without medical complications in pregnancy.

Multiple standardized scales were used to measure anxiety symptoms in the research articles under review. Group one studies used Beck Anxiety Inventory (BAI) (Kender et al., 2016); Hospital Anxiety and Depression Scale (HAD) (Cetin et al., 2016), Hopkins Symptom Checklist (SCL) (Bjørk et al., 2015), and State Trait Anxiety Inventory (STAI) (Gupton et al., 2000; Barber & Starkey, 2015; Marquesim et al., 2015). Two articles conducted the Structured Clinical Interview for DSM-IV (SCID) to diagnose anxiety and related disorders (Fairbrother et al., 2016; Uguz et al., 2012). Among the group one studies (i.e., those relevant to research questions one and two), there were six that used self-report measures (Barber & Starkey, 2015; Bjørk et al., 2015; Cetin et al., 2016; 2015; Gupton et al.; Kender et al., 2016; Marquesim et al., 2015) 2000 and two that used a diagnostic interview. (Fairbrother et al., 2016; Uguz et al., 2012). Generalized Anxiety Disorder (GAD-7) (Byatt et al., 2014); Hospital Anxiety and Depression Scale (HAD) (Jing Chen et al., 2016; Peng Chiong Tan et al., 2016); and State Trait Anxiety Inventory (STAI)(Gourounti et al., 2015). Assessment timings varied, starting from the first trimester and ending at 36 months after delivery for all the studies.

### ***Reporting anxiety scores/diagnoses***

The studies used multiple measures to report anxiety levels. Out of twelve included studies, seven compared mean anxiety scores of pregnant women with and without medical complications (Barber & Starkey, 2015; Byatt et al., 2014; Cetin et al., 2016; Gourounti et al., 2015; Gupton et al., 2000; Jing Chen et al., 2016; Kender et al., 2016). Four articles reported the prevalence rates of anxiety disorders in these women using the cut-off scores of the measurement scale (Bjørk et al., 2015; Marquesim et al., 2015; Peng Chiong Tan et al., 2016; Uguz et al., 2012). It must be

noted that “prevalence is a measure of the burden of disease in a population in a given location and at a particular time, as represented in a count of the number of people affected” (Ward, 2013, p. 1241). So these studies counted total number of women with high anxiety levels in the sample of all women having a medical complication and presented it as a percentage. One study compared the prevalence and incidence of anxiety and related disorders in high, medium and low-risk women, using Odds Ratios (Fairbrother et al., 2016). Incidence rates “represent the number of new cases of the disease among the number of susceptible persons in a given location and over a particular span of time” (Ward, 2013, p. 1241). Odds ratio (OR), on the other hand, is a commonly used measure of association reported in research studies (Zocchetti, Consonni, & Bertazzi, 1997). The study reported the odds that an anxiety disorder may occur given the presence of high-risk pregnancy, in one group of women and compared it to the odds of the anxiety occurring in the absence of that risk in other groups.

Among the eight group one studies only, six employed self-report measures of anxiety (Barber & Starkey, 2015; Cetin et al., 2016; Gourounti et al., 2015; Gupton et al., 2000; Jing Chen et al., 2016; Kender et al., 2016), whereas two employed diagnostic interviews (Fairbrother et al., 2016; Uguz et al., 2012). The group two studies all used self-report measures of anxiety ((Byatt et al., 2014; Gourounti et al., 2015; Jing Chen et al., 2016; Peng Chiong Tan et al). Table 13 presents an overall summary of the anxiety measurement scales and their results.

Table 13: Summary Self-Report Anxiety Measurement Scores

Study ID#	Measurement Tools	Cut-off anxiety scores	Statistical value/test	Results
3	STAI	Not given	p= <0.001	Mean Anxiety Scores: High-risk =42.3 (12.7) Low-risk= 34.4 (10.3)
4	SCL	Mean score >1.75	p= <0.001	Women with Epilepsy =22.4% Healthy Women =14.8%)
5	STAI	Low (20-30points) Moderate (31-49 points) High (>50 points)	chi-square p= <0.05	Trait Anxiety: HG=53(80%)and 55 (83.3%) NG=35(89.7%) and 35(89%)
6	STAI	Total score of 41 and above	t-test p= <0.001	Mean State Anxiety scores: Cases= 41.33 (12.12) Controls=37.48 (12.10)
7	HADS	Not given	ANOVA p= <0.001	Severe PE = 14.0(3.6) Mild PE= 5.4(3.1) Healthy women= 1.0(1.8)
8	STAI	Not given	p= <0.05	Mean Anxiety Scores High-risk =49.3 (11.6) Low-risk= 45.1 (8.8)
9	BAI	Not given	t-test p= <0.001	Mean Anxiety Scores HG= 19.22 (10.96) Control= 11.71 (8.21).
10	STAI	Not given	p= <0.05	Mean Trait Anxiety scores: T1=47.8 (5.1), T2= 43.3 (7.7) T3= 45.2 (8.5)
11	GAD-7	Total score of >10	p= <0.05	Mean Trait Anxiety scores: Initial =4.2 (6.5) Postpartum=5.2(5.1)
12	HADS	Total score of $\geq$ 9	ANOVA p= <0.001	Mean Anxiety Scores: 3.69 (2.76) 14 cases (7.18 %)

## **Thematic Analysis**

The data extracted from both groups of studies were analyzed in order to find answers for our three research questions.

### **Research questions 1 and 2:**

Eight studies comparing two groups of women (case-control design) were analyzed to answer the first two research questions. Anxiety symptoms were observed to be significantly higher among women experiencing a medically complicated pregnancy in comparison with those experiencing a medically uncomplicated pregnancy, in all eight studies (Barber & Starkey, 2015; Bjørk et al., 2015; Cetin et al., 2016; Gourounti et al., 2015; Gupton et al., 2000; Jing Chen et al., 2016; Kender et al., 2016; Peng Chiong Tan et al., 2016). Although these studies used different psychometric instruments, no study reported control groups having high anxiety scores.

With respect to the magnitude of this effect (research question two), a variety of outcome measures were reported, and as a consequence, summative statements cannot be made. Below I report on the findings of the individual studies. For each of the below, women experiencing a medically complicated pregnancy reported significantly higher anxiety compared with women experiencing a medically healthy pregnancy.

There were two case-control studies in which a diagnostic interview was administered, the following was reported (Fairbrother et al., 2016; Uguz et al., 2012). In the study by Uguz et al., the odds of meeting diagnostic criteria for one or more anxiety disorder was 4.13 for women experiencing hyperemesis gravidarum (HG; 36.5%) compared to women experiencing a normal, healthy pregnancy (12.2%). Fairbrother et al. (2016) report comparative, albeit slightly higher, findings. In their study, women experiencing a medically moderate or medically high risk

pregnancy, respectively, had a relative risk of 5.17 and 6.58 of meeting diagnostic criteria for a new onset anxiety disorder, compared with women experiencing a medically low risk pregnancy.

The remaining six studies assessed anxiety via self-report. Three of these assessed anxiety using the State Trait Anxiety Inventory (STAI; Barber & Starkey, 2015; Gupton et al., 2000; Marquesim et al., 2015). The studies conducted by Barber & Starkey (2015) and Gupton et al. (2000) both used the State version of the STAI, and reported mean scores of 42.3 and 41.3 among women experiencing pregnancy complications, and mean scores of 34.4 and 37.5 among women experiencing a normal, low risk pregnancy, respectively. The study by Marquesim et al. (2015) employed the Trait version of the STAI and found that a greater proportion of the women experiencing diabetes mellitus (25.8%) compared with those with normal glucose levels (7.7%), obtained anxiety scores in the severe range. Consistent with this, Bjork et al. (2015) also reported that a significantly greater proportion of pregnant women with epilepsy (22.4%) compared to women experiencing a normal, low risk pregnancy (14.8%) evidenced high levels of anxiety or depression, as measured via the SCL. Cetin et al. (2016) reported HADS-A (anxiety) mean scores of 14.0 among women experiencing severe preeclampsia, 5.4 among women experiencing mild preeclampsia, and 1.0 among women experiencing a medically healthy pregnancy. Finally, Kender et al. (2016) reported higher BAI scores among women experiencing hyperemesis gravidarum (19.2) compared with women experiencing a medically healthy pregnancy (11.7).

### **Research question 3:**

Six of the 12 included studies reported the prevalence of anxiety (either by diagnostic interview or questionnaire), among women experiencing a medically complicated pregnancy (Byatt et al., 2014; Bjørk et al., 2015; Jing Chen et al., 2016; Marquesim et al., 2015; Peng Chiong Tan et al., 2016; Uguz et al., 2012). Among these, prevalence estimates ranged from 7.8% (Jing

Chen et al., 2016) to 46.9% (Peng Chiong Tan et al., 2016). Specifically, the following prevalence estimates were reported for each of the six studies: 7.8% (Jing Chen et al., 2016), 13.1% (Byatt et al., 2014), 22.4% (Bjørk et al., 2015), 25.8% (Marquesim et al., 2015), 36.65% (Uguz et al., 2012), and 46.9% (Peng Chiong Tan et al., 2016). It is worth noting that there was significant variability in the timing of the assessments, and in the instruments used.

Three prevalence studies (group two) compared anxiety symptoms at various intervals among women with a high-risk pregnancy and reported highest levels at initial assessment; the symptoms decreased over time. The anxiety scores were 47.8 to 45.2 on Trait Anxiety scale (Gourounti et al., 2015), and 3.69 to 2.69 on HAD (Jing Chen et al., 2016), whereas the third study (Byatt et al., 2014) compared mean anxiety scores of GAD-7 at initial survey (5.2) and postpartum (4.2). Also, all four studies in group two showed a co-existence of depression in the high-risk pregnant women. 37.3% of participants fulfilled the criteria for both anxiety and depression caseness. (Peng Chiong Tan et al., 2016), 27% of participants had symptoms of depression (Byatt et al., 2014), 53.4% women had EPDS scores > 11. for depression (Gourounti et al., 2015), and 5.13% of high-risk women had depression (Jing Chen et al., 2016).

### ***Socio-demographic factors***

The relationship between various characteristics described in both groups of studies were also assessed to further answer the third research question. Six out of eight case-control studies (group one) found that pregnant women with medical complications were not socio-demographically different from other pregnant women whereas two studies provided no such details. The majority of the women in both groups were married or living with a partner and educated. However, interestingly, the two largest case-control studies (Barber & Starkey, 2015; Gupton et al., 2000) and the only population data cohort study (methodologically robust) (Bjørk

et al., 2015) showed that women with a medical complication more often had low household income, little education, and had more unplanned pregnancies compared to women without a medical complication. Also, more women in the hospitalized group had indigenous ethnicity when compared to the healthy pregnant women; who were predominantly white. The proportion of older women was higher in the groups with hyperglycemia than in the control group as shown by the only study on pregnant women with diabetes mellitus (Kender et al., 2016).

### ***Medical complications***

The general high-risk studies (from both groups one and two) had commonalities regarding reported risk factors (Barber & Starkey, 2015; Byatt et al., 2014; Fairbrother et al., 2016; Gourounti et al., 2015; Gupton et al., 2000; Jing Chen et al., 2016). Women in these studied had: a history of stillbirth or fetal mortality, preterm rupture of membranes, pre-eclampsia, placenta previa, placental abruption, gestational diabetes. Isolated diseases included hyperemesis gravidarum (Kender et al., 2016; Peng Chiong Tan et al., 2016; Uguz et al., 2012), epilepsy (Bjørk et al., 2015), preeclampsia (Cetin et al., 2016), and diabetes mellitus (Marquesim et al., 2015).

### **Risk of Bias/Quality Assessment**

The studies were assigned with an overall rating based on the tool derived from Newcastle-Ottawa Scale (NOS) (Wells et al., 2009); selected for quality assessment (Appendices A &B). Four criteria were used to appraise each study: (1) the appropriateness of the study design to answering the review question, (2) the presence of potential selection bias, (3) the validity of data collection methods, and (4) the appropriateness of data analysis to the research question.

These four criteria categories contributed to the assessment of study strength, producing a final rating of strong, moderate, or weak. An attempt was made to tabulate these characteristics for the studies included assessed. This scale has been adapted from the Newcastle-Ottawa Quality

Assessment Scale for case-control and prevalence studies, to perform a quality assessment for the systematic review. Each item got awarded a score from 0-2, with 2 representing the highest quality and 0 representing the lowest quality. The case-control studies were ranked from a total score of 18 whereas cohort studies were ranked out of a total score of 16.

Of the twelve studies of the prevalence of anxiety in high-risk pregnancies, four received an overall 'STRONG' rating, five were classified as 'MODERATE', and three were given an overall rating of 'WEAK' quality. Regarding design, there was little to distinguish between the studies in terms of appropriateness (all were either cohort or case-control designs, which were appropriate given the nature of the population being studied), and relevance (studies were selected for relevance early in the review by the application of inclusion criteria). Of the studies that utilized diagnostic interviewing as the method of anxiety assessment, blinding was not explicitly indicated. However, the majority of studies recruited a control group of women with a healthy pregnancy to strengthen their comparison. The overall study weighting was dictated by the criteria of the modified assessment, as described above. To summarize the results, it can be concluded that most of the included studies had methodological issues and could not be declared to be bias-free.

## Chapter 5: Discussion

This review provides preliminary evidence regarding the association between anxiety symptoms/anxiety disorders, and medical complications in pregnancy. This study aims to synthesize and evaluate the findings from quantitative studies assessing the anxiety symptoms and anxiety-related disorders in pregnant women diagnosed with medical complications.

The search results of this review revealed that only a small body of relevant literature was published in the last two decades. However, it is interesting to know that research is being conducted all over the world, and that this critical area is catching the international mental health researchers' attention. Among the available studies, only some used standardized psychological assessment tools to measure anxiety symptoms: most frequently by the State-Trait Anxiety Inventory followed by Hospital Anxiety and Depression Scale. All of the included studies used self-reporting scales to compare anxiety in women with and without a medical complication, except for two which conducted diagnostic interviews.

All eight studies that compared two groups of women (group one studies) were analyzed to answer the first and second research questions: what are the levels of anxiety symptoms and/or a likelihood of a diagnosis of an anxiety or related condition, among women experiencing a medically complicated pregnancy compared to the healthy pregnant women, and what is known about the magnitude of this difference? In the results, the anxiety symptoms were observed to be significantly higher among women with a medical complication in comparison to those without a complicated pregnancy, in all eight studies. No study reported control groups as having high anxiety scores. With respect to the magnitude of this effect, a variety of outcome measures were reported, and as a consequence, summative statements cannot be made. However, for all the psychometric scales and diagnostic tools, women experiencing a medically complicated pregnancy

reported significantly higher anxiety compared with women experiencing a medically healthy pregnancy.

The above mentioned results are in line with the findings of previous researchers of high-risk pregnancies whose work was not a part of this review. For example, Thiagayson and colleagues (2013) have found that antenatal anxiety disorders are highly prevalent in high-risk pregnant Singaporean women. Similarly, women with severe preeclampsia have reported a significantly higher level of anxiety symptoms than women with mild preeclampsia in another US study (Black, 2007). A research study by King et al. (2010) also found significantly higher anxiety scores in high-risk pregnant women compared to control women. However, among various measures of disease frequency, self-reported tools have the highest probability of research biases. Self-reported scores, calculated by a single psychometric instrument are not as reliable to estimate the burden of disease as the structured clinical interview (Reimers et al., 2012). Therefore our findings should be interpreted with caution.

To answer the third research question, prevalence studies (group two) compared anxiety symptoms at various intervals in women with a high-risk pregnancy and three reported highest levels at initial assessment; the symptoms decreased over time. These studies reported the prevalence rates of the anxiety symptoms among these women to range between 7.8% to 46.9%, at various assessment times. Variation existed in the magnitude of the difference in prevalence rates. Prevalence is the probability of a disease for a population member at a point in time (Ward, 2013). Therefore, it is a way of assessing the overall burden of disease in the population, and a useful measure for administrators to determine the need for treatment facilities. But again, other more extensive studies using multiple psychometric instruments, like Thiagayson et al. (2013), and Adouard et al. (2005), have reported the prevalence of anxiety symptoms in high-risk women

to be around 13%. The variation in anxiety levels found in this review might be explained by the difference in the nature and scope of the included research. As reported earlier (Table 13) these studies used a single psychometric instrument; none of them used a pregnancy-specific anxiety instrument. Moreover, the sample sizes were smaller, and the selection process was not bias-free.

Similarly, it is difficult to ascertain how prevalent individual anxiety and related disorders are among this population as only two of the included studies used DSM-IV criteria. Nonetheless, both the authors have concluded that the risk may be most significant for two disorders: obsessive-compulsive disorder (OCD) and generalized anxiety disorder (GAD). Though no previous published research is available to endorse these findings, the results suggest that GAD and OCD are important psychiatric illnesses, which need to be evaluated in women who are more vulnerable due to a complicated pregnancy. One possible explanation of high likelihood of these two disorders could be that, during the perinatal period, reported rates of GAD and OCD are higher than in the general population (Leach et al., 2017).

The prevalence studies (group two) also indicated that anxiety symptoms were highest at initial assessment; they decreased throughout hospitalization. This finding may be explained by the decrease in maternal stress as a high-risk pregnancy progresses smoothly. There might be an increase of optimism regarding the pregnancy outcome (low probability of fetal complications) leading to the plummet in anxiety scores, over time. Clauson (1996) in a study of high-risk pregnancies demonstrated that most of the pregnant women had moderate levels of uncertainty at hospital admission and uncertainty levels lowered significantly at the time of discharge. Also, all four studies showed a co-existence of depression in the high-risk pregnant women. This finding is endorsed by the work of past researchers who confirmed that mood and anxiety disorders were highly prevalent in women with a complicated pregnancy, such as Thiagayson et al. (2013).

Overall, high anxiety rates found in this review can also be linked with the added stress of medical management of the disease. As most of the high-risk women were hospitalized, during or before the data collection, it may be inferred that hospitalization itself impacted the quality of their life. These obstetric inpatients might have experienced a lower quality of life than those healthy pregnant women who were not hospitalized; this experience causing additional anxiety. These findings are supported by the work of Nakamura and colleagues (2012) in the Japanese study of stress among hospitalized pregnant women. Maloni, Margevicious, and Damato (2006) have also presented a positive association between hospitalization and bed rest with maternal stress levels. Similar findings are shown by other studies as well (Maloni et al., 2002).

Another interesting finding, coming from three large and methodologically robust studies, is that women with a medical complication more often had low household income, little education, and had more unplanned pregnancies compared to women without a medical complication. Also, more women in the hospitalized group had indigenous ethnicity, compared to the healthy pregnant women who were predominantly white. The association between socioeconomic status and the mental health of women has been described in the past (Lund et al., 2010). Similarly, higher levels of education are found to be protective, particularly for women, against depression (Ploubidis & Grundy, 2009). Moreover, Paradies (2006) has explained how racism permeates the cultural contexts of social life through ethnocentric cultural models of racist attitudes, structural barriers to opportunities and, discriminatory treatment. Endorsing our findings, the persistence of significant disparities in health indicators, mediated by race and ethnicity, are reported by minority health researchers (Williams, Costa, Odunlami, & Mohammed, 2008).

The results of the quality assessment process of all the included studies are also another important consideration. On the adapted version of the Newcastle-Ottawa Quality Assessment

Scale for case-control and cohort studies, all twelve studies were evaluated: four received an overall 'STRONG' rating, five were classified as 'MODERATE', and three were given an overall rating of 'LOW' quality. Hence the probability of bias in the study design, sample selection, data analysis and conclusion can not be ruled out. As according to Wilson and Lipsey (2001), variability in the quality of studies may account for variability in the results of a systematic review

In the end, anxiety research is an evolving field, and unlike depression, few studies have been conducted in high-risk pregnant women. However, the bulk of available research literature, on anxiety in women with medically complicated pregnancies, is consistent with the findings of this review. As Dulude, Belanger, Wright, and Sabourin (2002) have demonstrated, expectant mothers with high-risk pregnancies suffer from "emotional instability and heightened anxiety" (p. 102). The findings of the current review suggest that within a high-risk condition, the prevalence of anxiety symptoms is high among pregnant women. To present a summary, the review findings are consistent with some aspects of available literature on medically complicated pregnancies. though, the evidence about some other dimension is not conclusive. It is likely that some inconsistencies in our findings are due to methodological differences; self-reported scales of anxiety symptoms and small sample sizes.

## **Conclusion**

The findings of the current review suggest that there is a scarcity of literature on anxiety and related disorders among women experiencing a medically complicated pregnancy. However, within a high-risk condition, the prevalence of anxiety symptoms is high among pregnant women. Most of the women experiencing a medically complicated pregnancy have significantly higher levels of anxiety symptoms compared to the pregnant women in the low risk or healthy group. However, an exact estimate of anxiety prevalence or incidence among these women cannot be

provided due to the methodological differences in the included studies. Some studies reported the prevalence rates of the anxiety symptoms to be of highest levels at initial assessment; the symptoms decreased over time. Some evidence for high-risk women's low household income, low education, more unplanned pregnancies, and indigenous ethnicity, compared to women without a medical complication, is also there. It is important to mention that based on the overall quality of the available studies, the findings cannot be considered bias-free.

### **Implications for Clinical Practice**

Although a small number of studies, and the heterogeneity in findings, remain a concern, we have evidence from this review that supports the presence of a higher level of anxiety symptoms in women experiencing a medically complicated pregnancy. Therefore, it is important that anxiety and related disorders be routinely investigated during all pregnancies and more importantly during the medically complicated ones. Moreover, just like depression and other diseases, interventions made in due time to deal with these disorders may greatly improve the quality of mental health during pregnancy. It is staunchly recommended to support and implement anxiety screening/prevention programs, specifically in pregnant women with other high-risk medical conditions. Such interventions are shown to reduce the symptoms of anxiety and related disorders in community women. Although there may be some practical issues around adding anything extra into already burdened obstetric units, antenatal clinics are probably the sites of choice if anxiety prevention programs are to be rolled-out successfully. The psychiatrists and obstetricians must work together to improve the healthcare delivery among this vulnerable population.

### **Suggestions for future researchers**

Based on this literature review, perinatal anxiety in complicated pregnancies is found to be a highly under-researched area. There is a scarcity of high quality diagnostic studies and many

instruments are being used to measure anxiety symptoms. Agreement on a few “gold standards” for measuring perinatal anxiety still remains elusive. Moreover, the majority of the instruments measure anxiety symptoms but not the functional impairment and quality of life of the women and their family members. Therefore, more controlled research, including meta-analytic studies, is needed in this field.

Therefore, it is strongly suggested that large population studies be conducted to find out the actual burden of anxiety and related disorders in pregnant women. The use of gold standard diagnostic interview (whenever possible) or employing validated instruments for early detection of anxiety and related disorders in women with medically complicated pregnancies is the key to achieving reliable evidence. It is also desired that in future larger samples where medical records are obtained for included pregnant are drawn. The identification of contexts as well as various influencing factors on anxiety prevalence during pregnancy is also required by longitudinal research, using multidimensional approaches. Whilst there is a considerable gap in the current literature, we can still state that the human and capital cost of anxiety disorders is high among pregnant women; who are under additional stress from medical complications. To reduce costs, future studies should target effective anxiety screening programs and fill these gaps in perinatal mental health literature.

### **Limitations**

I begin by revealing flaws in this work, caused by the small number of articles available on anxiety disorders in medically high-risk pregnancies. Firstly, despite a clear presentation of higher anxiety rates/ diagnoses in women experiencing medically complicated pregnancies, the results are still unreliable. The small sample sizes, self-reporting bias and differences in methodologies contribute to a situation in which statistical analysis of the results is complicated.

Generalizability is difficult because of self-reported scales of anxiety symptoms and small sample sizes. Another limitation is that not all the included studies have used a control group of healthy pregnant women to compare the anxiety symptoms among the high-risk pregnant and the low-risk pregnant women. Anxiety, in most studies, was assessed using only one scale which was not valid to diagnose an anxiety disorder whereas the studies using a diagnostic interview were only two in number. Moreover, the literature was not available on many issues including psychological implications, social factors and actual clinical significance associated with anxiety and related disorders in pregnant women who experience a medical complication.

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## Appendix A

### Newcastle-Ottawa Quality Assessment Scale

#### *Case control studies*

This scale has been adapted from the Newcastle-Ottawa Quality Assessment Scale for case-control studies to perform a quality assessment of case-control studies for the systematic review.

Scoring: Each item will be awarded a number from 0-2, with “a” representing the highest quality (i.e., a 2), and “c” representing the lowest (i.e., a 0). Based on the total score out of 18, each study will be rated as STRONG, MODERATE or WEAK.

#### **A) STUDY DESIGN**

##### **1) Inclusion/exclusion criteria for full sample**

- a) Well-defined and well-justified inclusion/exclusion criteria.
- b) Inclusion/exclusion criteria is poorly defined or inadequately justified or both.
- c) Inclusion/exclusion criteria is missing or very problematic.

##### **2) Assessment of medical risk in pregnancy**

- a) Medical risk in pregnancy was independently assessed via primary medical record.
- b) Medical risk in pregnancy was ascertained via secondary sources (e.g., record linkage, self-report).
- c) Assessment of medical risk in pregnancy is not defined / very problematic / unable to ascertain.

#### **B) SELECTION BIAS**

##### **1) Representativeness of the cases**

- a) Consecutive or obviously representative series of cases.
- b) Some potential for selection biases.
- c) Significant potential for selection biases / not stated / unable to ascertain.

##### **2) Representativeness of the controls**

- a) Controls are representative of the general community of pregnant women.
- b) Some evidence controls may not be representative of the general community of pregnant women.
- c) Not representative / unable to ascertain.

##### **3) Comparability of cases and controls**

- a) Cases and controls appear identical in all ways other than medical risk in pregnancy.
- b) Cases and controls may differ in some small ways, other than medical risk in pregnancy.
- c) Significant differences between cases and controls / unable to ascertain case/control similarity.

#### **C) DATA COLLECTION**

**1) Assessment of anxiety symptoms/diagnosis**

- a) Gold standard diagnostic interviews with blind assessment / psychometrically valid self-report measures with a well-validated cut-score.
- b) Gold standard diagnostic interviews without blinding to condition / some issues with either: (a) psychometric properties of the scale or (b) selection of the cut-score / reporting of information.
- c) Gold standard diagnostic interviews not used or unable to determine / psychometrically valid self-report measures with a well-validated cut-score not used / unable to determine.

**2) Response rate**

- a) Same response rate for both groups.
- b) Non-respondents described / some differences in response rate between groups.
- c) Differences in response rates between cases and controls are sufficient to invalidate findings / no information provided / unable to determine.

**D) DATA ANALYSIS**

**1) Appropriateness to the research question**

- a) Data analysis is well justified and appropriate to the research question / study design.
- b) Some concerns about the appropriateness of the analytic approach which may bias the findings and/or analytic approach is poorly described (i.e., unable to determine appropriateness).
- c) Analytic approach is inappropriate to the research question / study design, sufficient to invalidate findings, and/or not described.

**GLOBAL RATING**

Table A1: Quality Assessment Scale scoring table for case control studies

ITEM	SECTION	RATING	SCORE
<b>Study Design</b>			
	1. Inclusion/exclusion 2. criteria		
	3. Assessment of medical risk in pregnancy		
<b>Selection Bias</b>			
	1. Representativeness of cases		
	2. Representativeness of controls		
	3. Comparability of cases and controls		
<b>Data Collection</b>			
	1. Assessment of anxiety symptoms and diagnosis		
	2. Response rate		

<b>Data Analysis</b>			
	1. Appropriateness to the research question		
<b><i>Overall</i></b>			

## Appendix B

### Newcastle-Ottawa Quality Assessment Scale

#### *Prevalence studies*

This scale has been adapted from the Newcastle-Ottawa Quality Assessment Scale for cohort studies to perform a quality assessment of cross-sectional studies for the systematic review.

Scoring: Each item will be awarded a number from 0-2, with “a” representing the highest quality (i.e., a 2), and “c” representing the lowest (i.e., a 0). Based on the total score out of 16, each study will be rated as STRONG, MODERATE or WEAK.

#### **A) STUDY DESIGN**

##### **1) Inclusion/exclusion criteria for full sample**

- a) Well-defined and well-justified inclusion/exclusion criteria.
- b) Inclusion/exclusion criteria is poorly defined or inadequately justified or both.
- c) Inclusion/exclusion criteria is missing or very problematic.

##### **2) Assessment of medical risk in pregnancy**

- a) Medical risk in pregnancy was independently assessed via primary medical record.
- b) Medical risk in pregnancy was ascertained via secondary sources (e.g., record linkage, self-report).
- c) Assessment of medical risk in pregnancy is not defined / very problematic / unable to ascertain.

#### **B) SELECTION BIAS**

##### **1) Representativeness of the sample**

- a) Truly representative of the average in the target population. (random sampling)
- b) Somewhat representative of the average in the target population. (non-random sampling)
- c) Non-representative/no description of the sampling strategy.

##### **2) Comparability of respondents and non-respondents**

- a) Respondents and non-respondents appear identical in all ways other than medical risk in pregnancy.
- b) Respondents and non-respondents may differ in some small ways, other than medical risk in pregnancy.
- c) Significant differences between both groups / unable to ascertain

#### **C) DATA COLLECTION**

##### **1) Assessment of anxiety symptoms/diagnosis**

- a) Gold standard diagnostic interviews with blind assessment / psychometrically valid self-report measures.

- b) Gold standard diagnostic interviews without blinding to condition / Some issues with either:
  - (a) psychometric properties of the scale or (b) reporting of information.
- c) Gold standard diagnostic interviews not used or unable to determine / psychometrically valid self-report measures with a well-validated cut-score not used / unable to determine.

**2) Response rate**

- a) Same response rate for both groups.
- b) Non-respondents described / some differences in response rate between groups.
- c) Differences in response rates between cases and controls are sufficient to invalidate findings / no information provided / unable to determine.

**D) DATA ANALYSIS**

**1) Appropriateness to the research question**

- a) Data analysis is well justified and appropriate to the research question / study design.
- b) Some concerns about the appropriateness of the analytic approach which may bias the findings and/or analytic approach is poorly described (i.e., unable to determine appropriateness).
- c) Analytic approach is inappropriate to the research question / study design, sufficient to invalidate findings, and/or not described.

**GLOBAL RATING**

Table B1: Quality Assessment Scale scoring table for prevalence studies

ITEM	SECTION	RATING	SCORE
<b>Study Design</b>			
	1. Inclusion/exclusion criteria		
	2. Assessment of medical risk in pregnancy		
<b>Selection Bias</b>			
	1. Representativeness of cases		
	2. Comparability of respondents and non-respondents		
<b>Data Collection</b>			
	1. Assessment of anxiety symptoms and diagnosis		
	2. Response rate		
<b>Data Analysis</b>			
	1. Appropriateness to the research question		
<b>Overall</b>			

## Appendix C

### Quality Assessment

#### *Case control studies*

Table C1: Study 1 quality assessment

ITEM	SECTION	RATING	SCORE
<b>Study Design</b>			
	1. Inclusion/exclusion criteria	a	2
	2. Assessment of medical risk in pregnancy	a	2
<b>Selection Bias</b>			
	1. Representativeness of cases	a	1
	2. Representativeness of controls	a	1
	3. Comparability of cases and controls	a	2
<b>Data Collection</b>			
	1. Assessment of anxiety symptoms and diagnosis	a	2
	2. Response rate	a	2
<b>Data Analysis</b>			
	1. Appropriateness to the research question	a	2
<b>Overall</b>		<b>STRONG</b>	<b>16</b>

Table C2: Study 2 quality assessment

ITEM	SECTION	RATING	SCORE
<b>Study Design</b>			
	3. Inclusion/exclusion criteria	a	2
	4. Assessment of medical risk	a	2

	in pregnancy		
<b>Selection Bias</b>			
	4. Representativeness of cases	b	1
	5. Representativeness of controls	b	1
	6. Comparability of cases and controls	a	2
<b>Data Collection</b>			
	3. Assessment of anxiety symptoms and diagnosis	a	2
	4. Response rate	c	0
<b>Data Analysis</b>			
	2. Appropriateness to the research question	a	2
<b>Overall</b>		<b>MODERATE</b>	<b>12</b>

Table C3: Study 3 quality assessment

ITEM	SECTION	RATING	SCORE
<b>Study Design</b>			
	1. Inclusion/exclusion criteria	a	2
	2. Assessment of medical risk in pregnancy	a	2
<b>Selection Bias</b>			
	1. Representativeness of cases	b	1
	2. Representativeness of controls	b	1
	3. Comparability of cases and controls	b	1
<b>Data Collection</b>			
	1. Assessment of anxiety symptoms and diagnosis	a	2
	2. Response rate	c	0

<b>Data Analysis</b>			
	1. Appropriateness to the research question	b	1
<b>Overall</b>		MODERATE	10

Table C4: Study 4 quality assessment

<b>ITEM</b>	<b>SECTION</b>	<b>RATING</b>	<b>SCORE</b>
<b>Study Design</b>			
	1. Inclusion/exclusion criteria	a	2
	2. Assessment of medical risk in pregnancy	a	2
<b>Selection Bias</b>			
	1. Representativeness of cases	c	0
	2. Comparability of respondents and non-respondents	c	0
<b>Data Collection</b>			
	1. Assessment of anxiety symptoms and diagnosis	a	2
	3. Response rate	c	0
<b>Data Analysis</b>			
	1. Appropriateness to the research question	a	2
<b>Overall</b>		WEAK	8

Table C5: Study 5 quality assessment

<b>ITEM</b>	<b>SECTION</b>	<b>RATING</b>	<b>SCORE</b>
<b>Study Design</b>			
	1. Inclusion/exclusion criteria	a	2
	2. Assessment of medical risk in pregnancy	a	2
<b>Selection Bias</b>			

	1. Representativeness of cases	a	2
	2. Comparability of respondents and non-respondents	a	2
<b>Data Collection</b>			
	1. Assessment of anxiety symptoms and diagnosis	a	2
	2. Response rate	a	2
<b>Data Analysis</b>			
	1. Appropriateness to the research question	a	2
<b>Overall</b>		<b>STRONG</b>	<b>14</b>

Table C6: Study 6 quality assessment

ITEM	SECTION	RATING	SCORE
<b>Study Design</b>			
	1. Inclusion/exclusion criteria	b	1
	2. Assessment of medical risk in pregnancy	b	1
<b>a. Selection Bias</b>			
	1. Representativeness of cases	b	1
	2. Representativeness of controls	b	1
	3. Comparability of cases and controls	b	1
<b>Data Collection</b>			
	1. Assessment of anxiety symptoms and diagnosis	a	2
	2. Response rate	c	0
<b>Data Analysis</b>			
	1. Appropriateness to the research question	a	2
<b>Overall</b>		<b>WEAK</b>	<b>9</b>

Table C7: Study 7 quality assessment

ITEM	SECTION	RATING	SCORE
<b>Study Design</b>			
	1. Inclusion/exclusion criteria	a	2
	2. Assessment of medical risk in pregnancy	a	2
<b>Selection Bias</b>			
	1. Representativeness of cases	a	2
	2. Comparability of respondents and non-respondents	a	2
<b>Data Collection</b>			
	1. Assessment of anxiety symptoms and diagnosis	a	2
	2. Response rate	a	2
<b>Data Analysis</b>			
	1. Appropriateness to the research question	a	2
<b>Overall</b>		<b>STRONG</b>	<b>14</b>

Table C8: Study 8 quality assessment

ITEM	SECTION	RATING	SCORE
<b>Study Design</b>			
	1. Inclusion/exclusion criteria	a	2
	2. Assessment of medical risk in pregnancy	a	2
<b>Selection Bias</b>			
	1. Representativeness of cases	b	1
	2. Representativeness of controls	b	1
	3. Comparability of cases and controls	a	2
<b>Data Collection</b>			

	1. Assessment of anxiety symptoms and diagnosis	a	2
	2. Response rate	c	0
<b>Data Analysis</b>			
	1. Appropriateness to the research question	a	2
<b>Overall</b>		<b>MODERATE</b>	<b>12</b>

*Prevalence studies*

Table C9: Study 12 quality assessment

<b>ITEM</b>	<b>SECTION</b>	<b>RATING</b>	<b>SCORE</b>
<b>Study Design</b>			
	1. Inclusion/exclusion criteria	a	2
	2. Assessment of medical risk in pregnancy	b	1
<b>Selection Bias</b>			
	1. Representativeness of cases	b	1
	2. Comparability of respondents and non-respondents	a	2
<b>Data Collection</b>			
	1. Assessment of anxiety symptoms and diagnosis	a	2
	2. Response rate	a	2
<b>Data Analysis</b>			
	1. Appropriateness to the research question	a	2
<b>Overall</b>		<b>STRONG</b>	<b>12</b>

Table C10: Study 9 quality assessment

ITEM	SECTION	RATING	SCORE
<b>Study Design</b>			
	1. Inclusion/exclusion criteria	a	2
	2. Assessment of medical risk in pregnancy	b	1
<b>Selection Bias</b>			
	1. Representativeness of cases	a	2
	2. Comparability of respondents and non-respondents	c	0
<b>Data Collection</b>			
	1. Assessment of anxiety symptoms and diagnosis	a	2
	2. Response rate	c	0
<b>Data Analysis</b>			
	1. Appropriateness to the research question	a	2
<b>Overall</b>		MODERATE	9

Table C11: Study 10 quality assessment

ITEM	SECTION	RATING	SCORE
<b>Study Design</b>			
	1. Inclusion/exclusion criteria	a	2
	2. Assessment of medical risk in pregnancy	a	2
<b>Selection Bias</b>			
	1. Representativeness of cases	b	1
	2. Comparability of respondents and non-respondents	c	0

<b>Data Collection</b>			
	1. Assessment of anxiety symptoms and diagnosis	a	2
	2. Response rate	c	0
<b>Data Analysis</b>			
	1. Appropriateness to the research question	a	2
<b>Overall</b>		<b>MODERATE</b>	<b>9</b>

Table C12: Study 11 quality assessment

<b>ITEM</b>	<b>SECTION</b>	<b>RATING</b>	<b>SCORE</b>
<b>Study Design</b>			
	1. Inclusion/exclusion criteria	a	2
	2. Assessment of medical risk in pregnancy	b	1
<b>Selection Bias</b>			
	1. Representativeness of cases	b	1
	2. Comparability of respondents and non-respondents	c	0
<b>Data Collection</b>			
	1. Assessment of anxiety symptoms and diagnosis	a	2
	2. Response rate	c	0
<b>Data Analysis</b>			
	1. Appropriateness to the research question	a	2
<b>Overall</b>		<b>WEAK</b>	<b>8</b>