A systematic review of the psychological impact of pregnancy-related illnesses in the perinatal period and testing a cognitive model to predict posttraumatic stress disorder in women following experiences of Hyperemesis Gravidarum

Thesis submitted in partial fulfilment of the requirement for

the degree of:

Doctorate of Clinical Psychology (DClinPsy)

South Wales Doctoral Programme in Clinical Psychology

Cardiff University

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Supervised by Dr Helen Penny and Dr Cerith Waters

20th May 2019
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DECLARATION

This thesis is the result of my own independent work, except where otherwise stated, and the views expressed are my own. Other sources are acknowledged by explicit references. The thesis has not been edited by a third party beyond what is permitted by Cardiff University's Use of Third-Party Editors by Research Degree Students Procedure.

Signed _________________________ Date 20th May 2019

STATEMENT 1

This thesis is being submitted in partial fulfilment of the requirements for the degree of Doctorate in Clinical Psychology (DClinPsych)

Signed _________________________ Date 20th May 2019

STATEMENT 2

This work has not been submitted in substance for any other degree or award at this or any other university or place of learning, nor is it being submitted concurrently for any other degree or award (outside of any formal collaboration agreement between the University and a partner organisation)

Signed _________________________ Date 20th May 2019

STATEMENT 3

I hereby give consent for my thesis, if accepted, to be available in the University’s Open Access repository (or, where approved, to be available in the University's library and for inter-library loan), and for the title and summary to be made available to outside organisations, subject to the expiry of a University-approved bar on access if applicable.

Signed _________________________ Date 20th May 2019

WORD COUNT 15,246 (Excluding summary, acknowledgements, declarations, contents pages, appendices, tables, diagrams and figures, references, bibliography, footnotes and endnotes)

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Thesis Summary

This thesis has been written in the format of three papers: a systematic review, an empirical paper and a critical reflection paper.

Pregnancy-related illnesses can negatively impact on the physical wellbeing of mother and the development of the baby. However, whether experiencing an acute pregnancy-related illness has an acute or chronic impact on the mental health of women in the perinatal period has not been explored. Paper one presents a systematic review of the psychological impact of pregnancy-related illnesses in the perinatal period.

Hyperemesis Gravidarum is a pregnancy illness that is associated with negative psychosocial outcomes and increased risk of psychological distress in pregnancy and the postnatal period. Paper two used a cross-sectional design to test Ehlers and Clark’s cognitive model (2000) to predict posttraumatic stress disorder in women following experiences of Hyperemesis Gravidarum.

Paper three presents a critical reflection on the thesis process and as such is not intended for publication. The implications of the research for clinical practice and the relevance for clinical psychology are discussed. Reflections on personal and professional development are also explored.
Acknowledgements

Firstly, I would like to thank Dr Helen Penny and Dr Cerith Waters for their knowledge, guidance, encouragement and containing supervision. I wish to acknowledge the helpful advice from Pregnancy Sickness Support and thank the participants who completed the study and have volunteered to help in disseminating the findings. Additionally, I would like to thank my elective clinical placement supervisor’s Dr Sarah Douglass and Dr Catriona Matthews for helping to manage my work stress levels and allowing me the opportunities to support women who have experienced pregnancy-related illnesses which motivated me to conduct the research.

Thank you to my cohort who have provided essential emotional support throughout the clinical training process. Especially “the Bristol girls” who have provided endless train journey entertainment.

Last but certainly not least, thanks to my husband Mike whose support, sense of humour and patience has been invaluable. The endless supply of giggles and cuddles on the sofa with our Labrador Barley and baby bump has been an antidote to stress.
Paper One: Systematic Review

A systematic review of the psychological impact of pregnancy-related illnesses in the perinatal period.

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Paper One has been prepared for submission to British Journal of Health Psychology

(see Appendix 1 for submission guidelines).

For ease of reading, figures and tables have been included in the text rather than in appendices.

Word Count = 5042 (excluding tables, figures and references)
Abstract

Purpose: Pregnancy-related illnesses can negatively impact on the physical wellbeing of mother and development of the baby. This systematic review aims to assess the impact of pregnancy-related illnesses on a mother’s mental health in the perinatal period.

Methods: Relevant literature was identified through MEDLINE, PsycINFO, EMBASE and CINAHL databases using predetermined search strategies grouped under three main headings: perinatal period, pregnancy-related illnesses and psychological impact. Studies identified were categorised according to pre-defined inclusion and exclusion criteria. The quality of included studies was reviewed by CASP appraisal tool for cohort studies.

Results: Nineteen studies met review criteria including studies focussed on Hyperemesis Gravidarum (HG), Gestational Diabetes Mellitus (GDM), Hypertensive Disorders of pregnancy (HDP), Anaemia and pregnancy-related pelvic or lumbar pain. Evidence of a relationship between HDP and postnatal depression was consistent, and the prevalence of posttraumatic stress disorder (PTSD) postnatally ranged from 10.5% to 17%. HG was consistently associated with depression and PTSD postnatally. The relationship between GDM and postnatal depression was inconsistent. Anaemia was associated with a 5.5% of women having depression at 4-6 weeks postnatally. Lumbopelvic pain and postnatal depression had a co-morbid prevalence of 10% at 3 months postnatally. These relationships were often associated with prenatal psychological distress, illness factors and associated obstetric complications.

Conclusions: Women who experience pregnancy-related illnesses are at increased risk for anxiety, depression and PTSD in the perinatal period.
Keywords: pregnancy-related illness; hyperemesis gravidarum; hypertensive disorders of pregnancy; gestational diabetes mellitus; postnatal depression; posttraumatic stress disorder; perinatal; mental health.

Practitioner Points

- Screening for depressive symptoms, anxiety and PTSD in antenatal appointments is essential to identify women at risk for psychological distress following pregnancy related illness.
- Healthcare professionals could intervene with psychologically informed treatment plans to alleviate reactive anxiety and to prevent a sense of helplessness and fear, which may lead to symptoms of PTSD.
- Future research should investigate the efficacy of psychological therapy for mental health conditions in the context of pregnancy-related illnesses.

Statement of contribution

What is already known on this subject?

Pregnancy-related illnesses negatively impact the physical and psychological health of women in the antenatal period. Pregnancy-related illnesses can result in secondary obstetric complications, which may put the mother and baby at risk.

What does this study add?

Pregnancy-related illnesses of HG, GDM, HDP, pregnancy-related anaemia and pelvic or lumbar pain adversely affects perinatal mental health in some women. The relationship between pregnancy-related illness and perinatal mental health is often associated with prenatal psychological distress, illness factors and associated obstetric complications.
Background

Pregnancy-related illnesses are medical conditions secondary to being pregnant, which adversely affect the physical health of the mother. Pregnancy-related illnesses can include **Hypertensive disorders of pregnancy (HDP)**, **Gestational diabetes mellitus (GDM)** and **Hyperemesis Gravidarum (HG)**. **Hypertensive disorders of pregnancy (HDP)** such as pre-eclampsia (PE), eclampsia (E) and/or the haemolysis, elevated liver enzymes and low platelets (HELLP) syndrome together impact 3% of pregnancies (Delahaije, Dirksen, Peeters & Smits, 2013). These hypertensive disorders of pregnancy range in severity and can be potentially life-threatening for both mother and baby (Porcel, Feigal, Poye & Postma, 2013). HDP have psychosocial and psychological consequences in pregnancy and postnatally (Engelhard, Van Rij, Boullart & Ekhart, 2002; Pampus, Wolf, Schultz, Neelman et al. 2004; Roes, Raijmakers, Schoonenberg, Wanner et al. 2005; Rep, Ganzevoort, Bonsel, Wolf, et al. 2007). **Gestational diabetes mellitus (GDM)** affects between 4% and 10% of pregnancies and can result in pregnancy and delivery complications, alongside long-term health risks (Ovesen, Jensen, Damm, Rasmussen et al. 2015). GDM has also been inconsistently associated with antenatal anxiety and antenatal and postpartum depression (Azami, Badfar, Solemani & Rahmati, 2019).

**Hyperemesis Gravidarum (HG)** is prolonged and excessive nausea and vomiting in pregnancy that can result in weight loss, ketonuria and dehydration that requires medical treatment and hospitalisation (RCOG, 2016). The reported incidence of 0.3–2% varies across ethnic groups and is dependent on diagnostic criteria (Einarson, Piwko, & Koren, 2013). The risk of recurrence in subsequent pregnancies is reported to be 15% (Vlachodimitropoulou-Koumoutsea, Gosh, Manmatharajah, Igwe-Omoke et al. 2013). Though this may be an
underestimation because HG is often not diagnosed or not treated by hospitalization. Extreme weight loss associated with HG can lead to maternal gallbladder and liver dysfunction, renal failure and premature delivery (Fejzo, Poursharif, Korst & Munch, 2009). Psychological distress has been evidenced in the antenatal period in pregnancies complicated by HG (Mitchell-Jones, Gallos, Farren, Tobias et al. 2017). Women who suffer pregnancy-related illnesses are at increased risk for anxiety, PTSD and depression in the perinatal period (Meltzer-Brody, Maegbaek, Medland, Miller et al. 2017; Grekin & O’Hara, 2014; Yildiz, Ayers & Phillips, 2017; Benute, Nomura, Reis, Fraguas et al. 2010; Furuta, Sandall, Cooper & Bick, 2014).

Mental health conditions affect approximately 15-20% of women in the perinatal period which includes pregnancy and the first year after birth (NICE, 2015; Bauer, Parsonage, Knapp, Lemmi et al. 2014). Perinatal mental health problems are a significant public health issue given the long-term adverse impact on both mother and child (Meltzer-Brody & Stuebe, 2014; Cook, Ayers & Horsch, 2018; Rees, Channon & Waters, 2019). Despite this, an estimated 40%-70% of women have no access to UK perinatal mental health services. The impact of perinatal mental health problems on mother and child has a total long-term cost to society of an estimated £8.1 billion for each 1-year cohort of births in the UK (Bauer et al. 2014).

A better understanding of the occurrence and severity of mental health problems following pregnancy-related illnesses may lead to improved preventive strategies and targeted interventions. Prevention and timely recognition of mental health conditions can reduce treatment duration and costs (Poel, Swinkels & de Vries, 2009). Untreated anxiety and depression can persist for years and can adversely affect infant development (Bonari, Pinto,
Ahn, Einarson et al. 2004), the couple’s relationship and the parent-baby bond (Parfitt & Ayers, 2009).

Previous systematic reviews have focused on the psychological impact of severe maternal morbidity (Furuta et al. 2014). There has been a rapidly evolving field into birth trauma including risk factors for, the prevalence of or treatment for PTSD following childbirth trauma (de Graaff, Honig, van Pampus, & Stramrood, 2018; Yildiz et al. 2017; Furuta, Horsch, Ng, Bick et al. 2018). Other systematic reviews have looked at the prevalence of maternal mental health in the perinatal period (Fisher, Mello, Patel, Rahman et al. 2012), risk factors (Furtado, Chow, Owais, Frey et al. 2018; Biaggi, Conroy, Pawlby & Pariante, 2016) or the impact of perinatal mental health on child outcomes (Cook et al. 2018; Rees et al. 2019). The effects of HG (Mitchell-Jones et al. 2017) and HDP (Delahaije et al. 2013) has been reviewed in the antenatal period. However, whether experiencing an acute pregnancy-related illness in pregnancy has an acute or chronic impact on mental health in women has not been reviewed, despite current research highlighting the importance of good physical and mental health in the perinatal period to prevent adverse biopsychosocial consequences for both mother and baby. Therefore, this systematic review aims to examine the differential impacts of pregnancy-related illnesses as independent risk factors for worsening mental health in the perinatal period.

**Method**

**Search strategy**

Studies were identified by systematically searching the following databases: EMBASE, Medline, PsycINFO and CINAHL. Database searches were restricted to human research
articles, written in English and published in peer-reviewed articles published in English from 1970 until February 2019.

Search terms were grouped under three main headings: perinatal period, pregnancy-related illnesses and psychological impact. These search terms included a combination of database-specific index terms (anxiety, depression, PTSD, perinatal period, name of illness) and specific terms as keywords and subject headings located in the title or abstract (Appendix 3).

Pregnancy-related illnesses were defined by guidelines for ‘pregnancy complications’ by the Centre for Disease, Control and Prevention (CDC, 2018), The Office on Women's Health (OWH, 2019), International Statistics Classification of Diseases and Related Health Problems (ICD-10, 2016) and Tommy’s Charity (2019). OWH also included miscarriage, ectopic pregnancy and foetal complications. These conditions were excluded from this review which focussed on pregnancy-related illness that changed the mother’s physical wellbeing such that they felt unwell with the symptoms (Appendix 2). Pregnancy illnesses searched included: HG, Anaemia, HDP (PE, HeLLP syndrome, PPROM), GDM, Sepsis, Uterine Infection, Peripartum cardiomyopathy, Chorioamnionitis and Pelvic and/or Lumbar pain.

**Inclusion criteria**

I. Primary research that focussed on the relationship between pregnancy-related illness and antenatal and/or postnatal mental health (e.g. PTSD, anxiety or depressive symptoms).

II. Mental health outcomes were measured using a questionnaire, interview, or clinical diagnosis during the perinatal period (from pregnancy to one year postpartum).

III. Observational studies and experimental studies with relevant data.
Exclusion criteria

I. The following study designs were excluded: systematic reviews, literature reviews, qualitative studies, conference abstracts, letters, commentary, news or short communication and repeated findings originated from the same research.

II. Studies with participants who were fathers.

III. Mothers who had experienced coma, cerebrovascular event, epilepsy or anaesthetic problems and/or PTSD resulting from pregnancy conflict, accidents or natural disasters.

IV. Studies that focussed on mental health outcomes associated with miscarriage, abortion, stillbirth or neonatal death. Or studies that did not analyse these participants separately.

V. Studies that reviewed the psychological impact beyond the perinatal period

Search Results

The initial database searches identified 8914 articles. Secondary searches involved scanning the reference lists of studies included in the systematic review, accessing online citations, and manual searches of relevant journals. An additional 10 articles were identified through secondary searches. Experts in the field and primary authors were contacted for access to further publications which yielded no new relevant literature. After 996 duplicates were removed, 7928 papers remained for review. Evaluation of the title and abstracts according to the inclusion and exclusion criteria decreased the articles from 7928 to 84. Due to previous steps being conservative, several articles that did not meet the review criteria were retained for full-text review because titles and abstracts were not specific enough to judge for inclusion. Evaluation of the articles’ text reduced the 84 studies to 19 studies. A
second reviewer independently screened full-text articles, and any conflicts were discussed and resolved. Of the pregnancy-related illnesses included in the search terms, only a minority of illnesses were identified (HG, GDM, HDP, Lumbar and/or Pelvic pain and Anaemia). A PRISMA flow diagram reporting the final numbers is shown in Figure 1.
Figure 1: Systematic Review Process

Records identified by database searching (n=8914)
Records identified through secondary searches (n=10)

Duplicates removed (n=996)

Records screened (n=7928)
Records excluded (n=7844)

Total records excluded (n=65)

Reasons for exclusion:
- Predictors of pregnancy illness (n=10)
- Focussed on offspring (n=5)
- Post-partum illness/haemorrhage (n=8)
- Traumas associated with pre-term babies in NICU (n=7)
- Case studies (n=2)
- Qualitative studies (n=3)
- Focussed on psychological outcomes in pregnancy (n=4)
- Did not report psychological outcomes (n=5)
- Outcomes beyond the perinatal period (n=8)
- Literature reviews (n=3)
- Protocol study (n=1)
- No detail of when outcomes were measured (n=2)

Full text articles assessed for eligibility (n=84)

Record included for review (n=19)
Procedure and assessment of the quality of evidence

The process for this review followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses protocols (PRISMA, 2015). The Critical Appraisal Skills Programme (CASP, 2018) guidance, recommended for reviewing observational research was used to aid the appraisal of the included studies. The framework provides an appraisal tool for cohort studies across 12 quality domains with a series of prompt questions for each domain. In each domain, a response of ‘yes’, ‘no’, or ‘can’t tell’ is given. To aid the comparison of quality across studies, a score of two was given for ‘yes’ a score of one was given for ‘can’t tell’ (suggesting there is partial support for the quality domain) and a score of zero was given to ‘no’. Scores across domains were then summed to provide a maximum quality score of 23 (Rees et al. 2016) (Appendix 4 CASP quality scores of studies) The total quality score for each study is included in Table 2.

Table 1: Methodological characteristics of included studies
<table>
<thead>
<tr>
<th>Study</th>
<th>Location</th>
<th>Design</th>
<th>Participants</th>
<th>Sampling method and/or study</th>
<th>Inclusion</th>
<th>Exclusion</th>
<th>Quality Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kjeldgaard et al. 2017</td>
<td>Norway</td>
<td>Prospective cohort</td>
<td>n= 628-830 HG depending on time of assessment</td>
<td>Data collected as part of the Norway MoBa study (1998-2008).</td>
<td>HG defined as prolonged nausea and vomiting leading to hospitalisation before 25 GW</td>
<td>None</td>
<td>19</td>
</tr>
<tr>
<td>Christodoulou-Smith et al. 2011</td>
<td>USA California</td>
<td>Cross-sectional study</td>
<td>n=377 HG n=233 healthy controls</td>
<td>Submit medical records and complete online questionnaire. Selective sampling</td>
<td>Women who had a diagnosis of HG and treatment with IV fluids. Women with HG were asked to recruit a friend (control).</td>
<td>Women aged &lt;18 or &gt;50. Women with multiple or abnormal gestation</td>
<td>16</td>
</tr>
<tr>
<td>Kjeldgaard et al. 2018</td>
<td>Norway</td>
<td>Prospective cohort</td>
<td>n=574 no nausea n=813 mild nausea n=522 severe nausea n=20 HG</td>
<td>Data collected from Norwegian ABC (2008-2010) cohort.</td>
<td>Women recruited GW 17 ultrasound clinic</td>
<td>Women who did not complete the first three questionnaires.</td>
<td>19</td>
</tr>
<tr>
<td>Senturk et al. 2017</td>
<td>Turkey</td>
<td>Prospective cohort</td>
<td>n=207 HG n=177 healthy controls</td>
<td>Convenience sampling of patients at private hospital in Turkey (May 2013-September 2015)</td>
<td>HG diagnosis for the study group. No nausea or vomiting in the first 3 months of pregnancy for the control group. Complete SCL-90 by 12 GW</td>
<td>History of psychiatric illness or during the study period. Multiple pregnancy. Gastrointestinal, thyroid, parathyroid or liver pathology. Factors related to the pregnancy, which could trigger anxiety during the pregnancy or have a detrimental effect on the psychiatric status (e.g. abnormal screening tests, premature birth, intrauterine fetal mortality, postpartum hemorrhage)</td>
<td>19</td>
</tr>
<tr>
<td>Daniells et al. 2003</td>
<td>Australia</td>
<td>Prospective cohort</td>
<td>n=50 GDM n=50 non-GDM</td>
<td>Convenience sampling from Diabetes Centre (2000-2001)</td>
<td>GDM, singleton pregnancy, no previous diagnosis with GDM, tested after 26 GW, seen in the clinic both within 1 week of diagnosis and before 32 GW</td>
<td>Previous GDM, multiple pregnancy, non-English, developmental delay or presenting after 33 GW</td>
<td>13</td>
</tr>
<tr>
<td>Beka et al. 2017</td>
<td>Canada</td>
<td>Prospective cohort</td>
<td>n=12140 GDM n=314583 non-GDM</td>
<td>Population cohort study (April 2000-March 2009)</td>
<td>Diagnosis of GDM in women who delivered in Alberta, Canada.</td>
<td>Multiple births, &lt;18 years or &gt;54 years, not Alberta residents at time of delivery, pre-existing diabetes (type 1 or type 2) or missing information concerning GDM diagnosis</td>
<td>19</td>
</tr>
<tr>
<td>Zwolinska-Kloc et al. 2017</td>
<td>Poland</td>
<td>Prospective cohort</td>
<td>n=35 GDM n=35 non-GDM</td>
<td>Convenience Sampling of women at Warsaw University</td>
<td>Lack of psychiatric disorders according to MINI</td>
<td>None</td>
<td>12</td>
</tr>
<tr>
<td>Study</td>
<td>Location</td>
<td>Design</td>
<td>Participants</td>
<td>Sampling method and/or study</td>
<td>Inclusion</td>
<td>Exclusion</td>
<td>Quality Rating</td>
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<tr>
<td>Ruohomaki et al. 2018</td>
<td>Finland</td>
<td>Prospective cohort study</td>
<td>n=916 non-GDM, n=150 GDM</td>
<td>Data extracted from KuBiCo database in January 2017</td>
<td>GDM diagnosed by Finnish clinical guidelines.</td>
<td>Previous mental health issues or diagnosis of GDM or DM, multiple pregnancy, final trimester of pregnancy</td>
<td>20</td>
</tr>
<tr>
<td>Hinkle et al. 2016</td>
<td>USA</td>
<td>Prospective cohort study</td>
<td>n=81 GDM, n=81 non-GDM</td>
<td>Data collected from 12 USA clinical centres NICHDGFSS-Singleton cohort (2009–2013)</td>
<td>Women without pre-existing chronic diseases, medical conditions, psychiatric disorders or pre-pregnancy diabetes.</td>
<td>None</td>
<td>20</td>
</tr>
<tr>
<td>Varela et al. 2017</td>
<td>Greece</td>
<td>Prospective cohort study</td>
<td>n=117 GDM, No control group</td>
<td>Convenience sampling by obstetricians in Athens, Greece</td>
<td>Women in their third trimester of pregnancy of Greek origin or fluent in Greek language who had GDM.</td>
<td>Active psychotic symptoms, organic brain pathology or intellectual disability</td>
<td>12</td>
</tr>
<tr>
<td>Huang et al. 2015</td>
<td>USA</td>
<td>Prospective cohort study</td>
<td>1686 women who had either normal GT, impaired GT, isolated HG or GDM</td>
<td>Recruited at 1st prenatal appointment by convenience sampling</td>
<td>22 GW or less pregnant, singleton, no prior glucose related health problems</td>
<td>Type 1 and 2 diabetes</td>
<td>20</td>
</tr>
<tr>
<td>Kim et al. 2005</td>
<td>USA</td>
<td>Prospective cohort study</td>
<td>n=64 GDM, n=148 PIH, n=1233 unaffected gravidas</td>
<td>Convenience sampling of antenatal women in San Francisco Bay Area hospitals.</td>
<td>&gt;18 years of age spoke English, Spanish, or Cantonese; presented for prenatal care before 16 GW.</td>
<td>Women with both GDM and PIH and/or with multiple gestations</td>
<td>19</td>
</tr>
<tr>
<td>Hoedjes et al. 2011</td>
<td>Netherlands</td>
<td>Prospective cohort study</td>
<td>n=149 PE, No normotensive controls</td>
<td>Women recruited from 4 hospital sites. Convenience sampling</td>
<td>Age &lt;18, pregnancy complicated by PE, Dutch speaking</td>
<td>None</td>
<td>19</td>
</tr>
<tr>
<td>Englehard et al. 2002</td>
<td>Netherlands</td>
<td>Historical cohort study</td>
<td>n=18 preterm PE, n=29 preterm birth, n=23 term PE, n=43 uneventful term birth</td>
<td>Convenience sampling of women recruited through hospital records and asked to complete postal questionnaires.</td>
<td>PE group: delivery &lt;36GW and hospitalisation for a week. Controls: uneventful pregnancy and term delivery &gt;37 weeks.</td>
<td>&lt;18 years at delivery, illiterate in Dutch, or with pregnancy complicated by intrauterine foetal death</td>
<td>19</td>
</tr>
<tr>
<td>Stamrood et al. 2011</td>
<td>Netherlands</td>
<td>Prospective cohort study</td>
<td>n=63 PE, n=65 PRROM, n=65 controls</td>
<td>Convenience sampling of women via Hospital (PE/HELLP/PPROM) or midwifery practices (controls)</td>
<td>Pregnant women hospitalised with PE and severe PE (HELLP syndrome) or PRROM or Healthy controls with uneventful pregnancies</td>
<td>PE/PPROM: condition so critical that participants required immediate c-section All groups: multiple pregnancy, history of intrauterine foetal death, drug</td>
<td>20</td>
</tr>
<tr>
<td>Study</td>
<td>Location</td>
<td>Design</td>
<td>Participants</td>
<td>Sampling method and/or study</td>
<td>Inclusion</td>
<td>Exclusion</td>
<td>Quality Rating</td>
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</tr>
<tr>
<td>Mautner et al. 2009</td>
<td>Austria</td>
<td>Prospective cohort study</td>
<td>n=90 Total n=18 (20%) HDP n=11 (12%) GDM n=39 (36%) Preterm n=29 control</td>
<td>Convenience sampling of women in obstetric clinics (June 2006-August 2007).</td>
<td>Women with an intact pregnancy between 24 and 37 GW, German language skills, pregnancy complications that develop at the end of the second and the beginning of the third trimester: HDP, GDM and risk for preterm delivery. Control group of women who had uncomplicated pregnancies.</td>
<td>Complications during early pregnancy or pregnancy loss.</td>
<td>19</td>
</tr>
<tr>
<td>Blom et al. 2010</td>
<td>Netherlands</td>
<td>Prospective cohort study</td>
<td>n=71 PE No controls</td>
<td>Women enrolled on Generation Project.</td>
<td>Pregnant women, resident in the study area (Rotterdam), with an expected delivery date between April 2002 and January 2006.</td>
<td>None</td>
<td>21</td>
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<tr>
<td>Gutke et al. 2007</td>
<td>Sweden</td>
<td>Prospective cohort study</td>
<td>n=180 (67%) Lumbopelvic pain n=44 (16%) PGP n=29 (11%) Lumbar pain n=14 (5%) combined PGP and lumbar pain</td>
<td>Convenience sampling of women recruited from two antenatal clinics between GW 12 to 18.</td>
<td>Swedish-speaking women with an expected normal pregnancy (as determined by midwives)</td>
<td>Systemic locomotor system diseases, verified diagnosis of spinal problems in the previous 2 months, or previous spinal, pelvic, or femur surgery.</td>
<td>19</td>
</tr>
<tr>
<td>Goshtasebi et al. 2013</td>
<td>Iran</td>
<td>Prospective cohort study</td>
<td>n=36 anaemic n=218 non-anaemic</td>
<td>Convenience sampling of women recruited from prenatal clinic of Imam Hospital (February-December 2009).</td>
<td>Singleton and low-risk pregnancy and no history of antidepressant-use</td>
<td>Mothers who had stressful life-experiences, history of using antidepressant drugs and mental or physical disorders, maternal or neonatal complications of birth or low birth weight neonates</td>
<td>12</td>
</tr>
</tbody>
</table>
**Key to terms in Table 1 and Table**

**Pregnancy-related illnesses**: Gestational diabetes mellitus (GDM), Diabetes Mellitus (DM), Hyperemesis Gravidarum (HG), Nausea and Vomiting (NVP), Hypertensive Disorders of pregnancy (HDP), Pre-eclampsia (PE), Pelvic Girdle Pain (PGP), Lumbar Pain (LP), Haemolysis, elevated liver enzymes and low platelets (HELLP), Preterm premature rupture of membranes (PRROM), Pregnancy Induced Hypertension (PIH), Glucose Tolerance (GT), Neonatal intensive care unit (NICU). **Cohort studies**: National Institute of Child Health and Human Development Fetal Growth Studies-Singleton cohort (2009–2013) (NICHHDFGS), Norwegian Mother and Baby cohort (NMoBa), Norwegian Akershus Birth Cohort Study (ABC), Kuopio Birth Cohort (KuBiCO). **Outcome measures**: State-Trait Anxiety Inventory (STAI), The hospital anxiety and depression scale (HADS), Edinburgh Postnatal Depression Scale (EPDS), Patient Health Questionnaire (PHQ-9), Beck Depression Inventory (BDI) Centre for epidemiological studies depression scale (CES-D), Peritraumatic Dissociative Experiences Questionnaire (PDEQ), Response to Intrusions Questionnaire (RIQ), White Bear Suppression Inventory (WBSI), PTSD Symptom Scale (PSS). Mental Health Inventory (MHI-5), Hopkins Symptom Checklist-25 (SCL-25), ICD-9 and ICD-10-CA codes, Mini International Neuropsychiatric Interview (MINI). World Health Organization quality of life assessment instrument (WHOQOL-BREF), Symptom-checklist 90 (SCL-90), Short-form 36 Health Survey (SF-36). **Miscellaneous**: Health-Related Quality of Life (HRQL), Socio-economic status (SES), Generalised Estimated Equation modelling (GEE), Gestational week (GW), caesarean section (c-sec), Post-partum (PP), Blood Pressure (BP), Body Mass Index (BMI).

**Table 2: Study analyses, results and limitations**
<table>
<thead>
<tr>
<th>Study</th>
<th>Exposure</th>
<th>Outcome Measures</th>
<th>Covariates</th>
<th>Timing of assessment/s</th>
<th>Data analysis</th>
<th>Results</th>
<th>Limitations: sample, measures, mechanisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kjeldgaard et al. 2017</td>
<td>HG (low distress vs high distress) vs no HG</td>
<td>Hopkins Symptom Checklist (SCL-5)</td>
<td>SES, BMI, previous HG, KLTD, smoking, physical activity, pregnancy, pelvic pain, age and parity</td>
<td>GW 17 &amp; 30, week 6 PP and 18 months PP</td>
<td>GEE model adjusted for covariates</td>
<td>Significant difference in emotional distress between women with HG and controls in pregnancy and 6 weeks postnatally but not 18 months. Women hospitalised in both 1st and 2nd trimesters had significantly higher odds for postnatal emotional distress. History of depression increased risk 3.42 times for postnatal depression and anxiety.</td>
<td>Sample: women who were immigrants, younger, smokers, single and with shorter education were under-represented. Measures: self-report screening tools. Recall bias as HG assessed retrospectively. Mechanisms: Prenatal emotional distress was not measured so not adjusted for in analyses.</td>
</tr>
<tr>
<td>Christodoulou-Smith et al. 2011</td>
<td>HG vs no HG</td>
<td>PTSD-7 questions</td>
<td>Breastfeeding, absent from work or school, lost/quit jobs, marital and financial problems, ability to provide childcare</td>
<td>Participants enrolled in pregnancy and encouraged to complete after due date.</td>
<td>Chi-squared analysis compared between groups</td>
<td>18% (68/377) of women reported full PTSD and had significantly worse negative life outcomes, psychological and physical wellbeing compared to controls</td>
<td>Sample: self-selection bias for HG and control group. Online survey may bias more educated and higher income women. Measures: only part of PTSD spectrum explored by self-report. Mechanisms: not controlled for socio-demographic, obstetric or pre-existing mental health factors.</td>
</tr>
<tr>
<td>Kjeldgaard et al. 2018</td>
<td>No NVP vs Mild NVP vs severe NVP vs HG</td>
<td>SCL-25 EPDS MINI</td>
<td>Parity, previous PTSD, anxiety or depression, major life events, maternal age, education, obstetric complications, birth experience</td>
<td>8 weeks PP and 2 years PP</td>
<td>Multiple linear mixed modelling</td>
<td>Severe NVP and HG had statistically significantly higher PTSD scores than controls at 8 weeks. Two years after birth, only severe NVP had statistically significantly higher PTSD compared to controls.</td>
<td>Sample: n=20 for HG. Generalizability may be limited as only Norwegian-speaking women, mainly Caucasians, were included in the study. Measures: No established and validated instrument such as the Perceptions of Labour and Delivery Scale (Bailham et al. 2004) was used in the present study to measure subjective birth experiences. Mechanisms: follow-up assessment in perinatal period limited to 8 weeks.</td>
</tr>
<tr>
<td>Senturk et al. 2017</td>
<td>HG vs no HG</td>
<td>SCL90 EPDS</td>
<td>Age, gravida, parity, number of abortions, gestational week, marital status, family arrangement, pregnancy planned or not, level of</td>
<td>First trimester Postnatally</td>
<td>Bivariate Logistic Regression</td>
<td>The results showed a 6.5-fold increased probability of postpartum depression in cases with HG. Higher scores observed in the depression, obsession, anxiety and somatization parameters of the SCL-90-R in</td>
<td>Sample: Turkish small sample limits generalisability Measures: study does not define when EPDS was measured</td>
</tr>
<tr>
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<td>Danells et al. 2003</td>
<td>GDM vs no-GDM</td>
<td>STAI, MHI-5</td>
<td>Demographic (age, parity, marital status, privately insured, family history of Diabetes). Anthropometric (BMI, fasting glucose levels)</td>
<td>At diagnosis, 30 GW, 36 GW and 6 weeks PP</td>
<td>ANOVA, chi-squared tests, t-tests and odds ratios to compare between groups</td>
<td>Some women with GDM had reactive anxiety at the time of diagnosis. By week 36 and in the PP period, no differences in mental health between women with GDM and controls.</td>
<td>Sample: small sample size. Measures: self-reported screening tools. Mechanisms: pre-existing mental health not measured to check whether this impacts adjustment and coping with GDM diagnosis.</td>
</tr>
<tr>
<td>Beka et al. 2017</td>
<td>GDM according to medical-records vs non-GDM</td>
<td>ICD-9 and ICD-10-CA hospitalizations and outpatient visits</td>
<td>Age, overweight, smoking, rural residence, ethnicity, median household income, nulliparity, preeclampsia or eclampsia, neonatal death, NICU admission, prior chronic medical conditions and fiscal year.</td>
<td>2 years prior to pregnancy, each trimester of pregnancy, 1-year PP</td>
<td>GEE models adjusted for covariates</td>
<td>Compared to women without GDM, women with GDM did not have an increased risk for new-onset mental illness before pregnancy, antenatally and postnatally. Women who had experienced PE, c-sec were at an increased risk of postnatal depression.</td>
<td>Sample: no limitation Measures: administrative data (ICD10 codes or hospitalisation visit) may have over-estimated incidence of mental illness. Mechanisms: administrative data limits ability to adjust for confounding variables.</td>
</tr>
<tr>
<td>Zwolinska-Kloc et al. 2017</td>
<td>GDM (not described how defined) vs non-GDM</td>
<td>HADS, MINI</td>
<td>Age, education, marital status, pregnancy planned or unplanned</td>
<td>5th-8th month of pregnancy, 2nd week PP, 6th week PP, between 6th-7th months PP</td>
<td>T-tests</td>
<td>No statistically significant difference in mean scores on HADS between GDM and controls at any time point. Three women with GDM met criteria for major depression at 6 months PP.</td>
<td>Sample: small pilot study Measures: HADS is self-report screening tool. Mechanisms: research design did not measure or control for potential confounders such as anthropometric and obstetric data and psychological history.</td>
</tr>
<tr>
<td>Ruohomaki et al. 2018</td>
<td>GDM vs no GDM</td>
<td>EPDS</td>
<td>Maternal age at delivery, BMI in the first trimester relationship status nulliparity, smoking before pregnancy, gestational age at</td>
<td>GW 28 and 44- &amp; 8-weeks PP</td>
<td>Logistic Regression, adjusted for co-variates.</td>
<td>The prevalence rates of PP depression were 10.3% after adjusting for covariates. Risk of postnatal depression was 1.7x more likely if women had experienced GDM. 40.9% of women who had GDM also had depression in third trimester.</td>
<td>Sample: self-selection bias. Measure: self-report screening tool. Mechanism: Diagnosis of GDM may be considered a stressful life event but this was not measured.</td>
</tr>
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<tr>
<td>Hinkle et al. 2016</td>
<td>GDM vs healthy control</td>
<td>EPDS</td>
<td>Age, race/ethnicity, parity, GDM during a prior pregnancy, pre-pregnancy BMI, SES, Social support, stress and gestational weight gain</td>
<td>6 weeks PP</td>
<td>Log poisson regression model, adjusted for covariates</td>
<td>GDM was associated with an adjusted 4.62-fold increased risk of subsequent postnatal depression. Women who had depression in trimester 1 and 2 had increased risk of GDM by 3.2 times, suggesting interplay GT and depression.</td>
<td>Sample: no limitation Measure: EPDS score is based on self-report rather than objective clinical interview. Mechanism: Diagnosis of GDM may be considered a stressful life event but this was not measured.</td>
</tr>
<tr>
<td>Varela et al. 2017</td>
<td>GDM vs healthy control</td>
<td>EPDS</td>
<td>Education, employment status, household income, marital status. Planned pregnancy, number of pregnancies and number of children.</td>
<td>3rd Trimester and 1-week PP</td>
<td>Logistic Regression</td>
<td>Probable diagnosis of depression occurred for 12% of the sample during the antenatal assessment and 15.1% in the postnatal assessment.</td>
<td>Sample: relatively small to control for confounders. 20.51% of the sample had dropped out by postnatal assessment. Highly educated, urban Greek population so not generalisable to other demographics. Measure: EPDS needs assessing at multiple timepoints PP to improve score validity. Mechanism: pregnancy BMI not measured or controlled for.</td>
</tr>
<tr>
<td>Huang et al. 2015</td>
<td>Normal GT vs Impaired GT vs Isolated Hyperglycaemia vs GDM</td>
<td>EPDS</td>
<td>Age, race/ethnicity, education, nativity, parity, marital status, household income, history of depression prior to pregnancy, smoking, physical activity, BMI and changes in dietary factors between first 2 trimesters</td>
<td>27 GW and again at 6 months postnatally</td>
<td>Multivariable logistic regression adjusted for covariates</td>
<td>Pregnancy glycemic status was not significantly associated with elevated PP depressive symptoms. Compared with normal GT women, the association appeared stronger among women with IHG than among those with GDM or IGT. Depressive symptoms occurred in 9.6% sample in prenatal assessment and 8.4% at 6 months postnatal</td>
<td>Sample: Number of IGT and GDM women was small so difficult to note a modest association with postnatal depression. Measures: self-report screening tools. Mechanisms: difficult to establish the temporality of incident pregnancy hyperglycemia and incident prenatal depressive symptoms.</td>
</tr>
<tr>
<td>Kim et al. 2005</td>
<td>GDM vs unaffected gravidas.</td>
<td>SF-36, CES-D</td>
<td>Age, race, education, pre-pregnancy weight &amp; exercise, parity, prior history of GDM,</td>
<td>12 and 20 GW, 8-12 weeks PP</td>
<td>Logistic regression adjusted for co-variates</td>
<td>PIH: significant decline in vitality and self-rated health and increase in depressive symptoms from antenatal to postnatal</td>
<td>Sample: different sample sizes for GDM and PIH, so possibly underpowered for multivariate adjustment.</td>
</tr>
<tr>
<td>PIH vs. unaffected gravidas</td>
<td>Income level, alcohol use, presence of chronic disease, marital status, and cigarette use</td>
<td>period. GDM: no significant differences between GDM and non-GDM between the third trimester of pregnancy and at 8-12 weeks PP on any measures.</td>
<td>Measures: biased by self-report. Mechanisms: unable to determine if disease severity was associated with further changes in health status or whether pre-existing mental health issues confounded the results</td>
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<tr>
<td>Hoedjes et al. 2011</td>
<td>Mild PE vs Severe PE vs uneventful healthy pregnancy (control)</td>
<td>EPDS</td>
<td>Age, ethnicity, educational level, parity, multiple pregnancies, mode of delivery, gestational age at birth, birth weight, admission to NICU, perinatal death.</td>
<td>6, 12- and 26-weeks PP</td>
<td>Logistic regression analysis adjusted for cofounders</td>
<td>Women with severe PE more frequently reported postpartum depressive symptoms at 6 and 12 weeks postpartum, but women who had mild PE more frequently reported depressive symptoms at 26 weeks postpartum.</td>
<td>Sample: small sample of women with depression so low power to detect clinically meaningful difference. Measure: no preconception data on psychological distress or associated depression risk factors measured. Mechanisms: social support, self-efficacy and perceived stress were not measured but may have mediated the effect of age on coping. Short PP follows up so unable to determine temporal relationship between depression development following PE.</td>
</tr>
<tr>
<td>Englehard et al. 2002</td>
<td>PE preterm, PE term, healthy preterm or healthy term</td>
<td>BDI, PSS, PDEQ, RIQ, WBSI</td>
<td>Intrauterine foetal death. Gestational age, caesarean section and length of hospital stay. Peritraumatic reactions and post-traumatic factors.</td>
<td>12-15-month PP</td>
<td>Multiple Regression</td>
<td>Depression: At &lt;2 years after hospitalisation depression was more prevalent in PE preterm (33%) than PE term (26%), healthy preterm (24%) or healthy term (7%). PTSD: At &lt;2 years after hospitalisation PTSD was more prevalent in PE preterm (28%) than PE term (17%), healthy preterm (28%) or healthy term (0%).</td>
<td>Sample: small sample size Measures: self-report screening tools and bias in retrospective recall. Mechanisms: temporal relationship between mental health following PE is difficult to ascertain because of retrospective design.</td>
</tr>
<tr>
<td>Stamrood et al. 2011</td>
<td>PE/HELLP, PPROM, uneventful healthy pregnancies (controls)</td>
<td>PSS and BDI</td>
<td>Hospital admission of child, death of child, birthweight, caesarean section, gestational age and length of mother’s hospital stay. Psychiatric history.</td>
<td>6 weeks and 15 months PP</td>
<td>Hierarchical Multiple Regression</td>
<td>At 6 weeks PP depression was more prevalent in PE (10.5%), PPROM (11.3%) than healthy term (6.2%). At 15 months PP prevalence of depression decreased in all groups PE (6.8%), PPROM (3.2%) than healthy term (0%). PTSD: At 6 weeks PP PTSD was more prevalent in PE (10.5%), PPROM (17%) than healthy term (3.1%). At 15 months PP prevalence of PTSD decreased in all groups PE (11.4%), PPROM (3.2%) than healthy term (0%).</td>
<td>Sample: small sample size Measures: self-report and retrospective. Mechanisms: drop-out at follow up in PPROM group was related to depression levels in pregnancy history so follow up results may have under-represented prevalence of PTSD and depression in PPROM.</td>
</tr>
<tr>
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<tr>
<td>Mautner et al. 2009</td>
<td>4 groups: HDP, GDM preterm delivery and control (uncomplicated pregnancy)</td>
<td>WHOQOL-BREF, EPDS</td>
<td>Age, education, rural or urban living, migration status, mode of delivery, week gestation</td>
<td>GW 24, 37, 2nd, 5th day PP and 3-4 months PP</td>
<td>A two-factorial mixed-model ANOVA</td>
<td>Preterm group had statistically significant higher depression scores and lower HRQL scores on the physical domain during pregnancy than those without complications. HDP group showed the second most depressive symptoms. Physical and global HRQL improved and depressive symptoms decreased significantly from late pregnancy and early PP period to late PP.</td>
<td>Sample: small sample recruited from a single institution. Measures: Self-report screening tools. Mechanisms: the impact of pre-existing mental health issues, timing of assessments and diagnosis were not controlled for.</td>
</tr>
<tr>
<td>Blom et al. 2010</td>
<td>PE compared to obstetric complications (preterm birth, c-sec)</td>
<td>EPDS</td>
<td>Maternal educational level, ethnicity, age, general psychopathological symptoms, family income, family functioning, hospitalisation of baby.</td>
<td>During pregnancy (GW not noted) and 2 months PP</td>
<td>Logistic regression analysis adjusted for co-variates</td>
<td>The risk of postnatal depression significantly increased with the number of perinatal complications women experienced. PE was significantly associated with postnatal depression.</td>
<td>Sample: participants represented the healthier population, EPDS data was more complete for highly educated women, and representation of some perinatal complications was low. Measure: EPDS screens for PP depression symptoms rather than the condition itself. Mechanisms: those who had more complications may have had higher physical morbidity, increasing their risk for postnatal depression</td>
</tr>
<tr>
<td>Gutke et al. 2007</td>
<td>PGP and LP</td>
<td>EPDS</td>
<td>BMI, Pain Urinary Leakage</td>
<td>GW 12 to 18- and 3-months PP</td>
<td>Logistic Regression</td>
<td>The comorbidity of lumbopelvic pain and depressive symptoms was 10%. Depressive symptoms were more prevalent in women with lumbar pain (31%) versus women without lumbopelvic pain (9%); whereas for women with PGP, this comparison was significant only at the screening level of EPDS&gt;=10 (P = 0.01).</td>
<td>Sample: small LP group to compare to PGP and PGP and LP group. Measures: EPDS is a self-reported screening tool. Mechanisms: unmeasured possible covariates such as length of pain, disturbed sleep and pre-conception psychological distress may have impacted PP depression</td>
</tr>
<tr>
<td>Goshtasebi et al. 2013</td>
<td>Anaemia (defined as Hb &lt;10.5 g/dL) vs healthy controls</td>
<td>EPDS</td>
<td>Age, education, mode of delivery, gestational age at delivery</td>
<td>4-6-week PP</td>
<td>Binary Logistic Regression</td>
<td>The prevalence of PP depression according to EPDS was 5.5%. Binary logistic regression analysis showed that Hb &lt;11 g/dL at delivery would increase the chance of PP depression by 4.64 times.</td>
<td>Sample: small sample from an urban population of low socioeconomic status. Measure: EPDS is a self-reported screening tool. Mechanisms: temporal relationship between pregnancy and postnatal depression is difficult to evaluate due to lack of follow up beyond 6 weeks PP</td>
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</tbody>
</table>
Results

Quality of studies

Table 1 provides an overview of the quality ratings of the included articles. The quality of the studies varied from the lowest score of 12 (Varela et al. 2017; Goshtasebi et al. 2013) to a highest of 21 out of 23 (Blom et al. 2010) with higher scores indicating better quality. The studies were representative of the population drawn from, and the pregnancy-related illness was often clearly objectively described. However, as the sample sizes varied and represented highly educated and low ethnic diversity of women, the findings are not representative of all women who experience pregnancy-related illnesses.

Design

Table 2 provides an overview of the included studies. The studies recruited participants from a range of countries USA (n=4), Canada (n=1), Netherlands (n=4), Iran (n=1), Sweden (n=1), Austria (n=1), Greece (n=1), Finland (n=1), Poland (n=1), Norway (n=2), Turkey (n=1) and Australia (n=1). Most studies were prospective cohort studies, one was cross-sectional, and one was a historical cohort design. Four studies focussed on Hyperemesis Gravidarum (HG), seven focussed on Gestational Diabetes Mellitus (GDM), four focussed on Hypertensive Disorders of pregnancy (HDP), one on Anaemia, one on pregnancy-related pelvic/lumbar pain and two on a combination of GDM and HDP.

Participants

Sample sizes ranged from n=35 (Zwolińska-Kloc et al. 2017) to n=12,140 (Beka et al. 2018). Most samples were convenience in nature. Participants were recruited from population studies (n=5) hospital or obstetric clinics (n=9), prenatal clinics (n=4) and online (n=1). Although ethnic diversity was varied across studies, the inclusion criteria of most studies stipulated that the participants spoke the language of the study origin. Many studies reported that women were highly educated, thereby reducing socio-economic diversity. The
inclusion and exclusion criteria were described in 14 studies, and five studies did not clearly define these.

**GDM and perinatal mental health**

The psychological impact of having GDM was reviewed in seven studies. Of these, three studies found that GDM was associated with an increased likelihood having depression one week post-partum (Varela et al. 2017), six weeks postpartum (Hinkle et al. 2016), and eight weeks postpartum (Rhuomaki et al. 2018). These effects remained following adjustment for the influence of covariates. Varela et al. (2017) showed an increased risk of depression prevalence from 12% antenatally to 15.1% postnatally (Varela et al. 2017). However, the study quality was poor, so results are interpreted with caution. In contrast, four studies did not find an increased risk of antenatal depression or postnatal depressive symptoms measured at 2 weeks, 6 weeks, 6 or 12 months postnatally (Zwolinska-Kloc et al. 2017, Huang et al. 2016, Beka et al. 2017), however, one study found that some women with GDM had reactive anxiety at the time of diagnosis (Daniells et al. 2003). These inconsistent findings may reflect differences in population demographics, range in quality of studies, mental health assessment measures and clinical cut-off points and follow-up intervals. A recent meta-analysis of GDM and postnatal depression also found an inconsistent relationship (Azami et al. 2019). The studies on GDM were limited by not establishing the temporality of incident pregnancy hyperglycaemia or pre-pregnancy BMI (Varela et al. 2017; Zwolinka-Kloc et al. 2017; Beka et al. 2018) despite obesity being a well-documented risk factor for GDM (Oteng-Ntim & Doyle, 2012) and perinatal depressive symptomatology (Molyneaux, Poston, Ashurst-Williams & Howard, 2014).
GDM and HDP and perinatal mental health

Two studies reviewed health-related quality of life and depression, comparing women with GDM, HDP, preterm delivery and uncomplicated pregnancies (Kim et al. 2005 and Mautner et al. 2009). Both studies found were no clinically relevant differences between women with GDM or controls in health-related quality of life and depressive symptoms in pregnancy or post-partum despite a general improvement over time. Kim et al. 2005 found that women with pregnancy-related hypertension reported a significant decline in health-related quality of life and an increase in depressive symptoms from pregnancy to postpartum compared with unaffected women. Both studies showed that women with GDM or pregnancy-related hypertension were more likely to undergo caesarean section than unaffected women, but only women with hypertension were more likely to have preterm delivery than normotensive controls. There were inconsistencies in whether the mode of delivery partially mediated the decline in health-related quality of life and depression between both studies.

HDP and postnatal mental health

All studies showed that HDP was found to be associated with an increased risk of depression and/or PTSD postnatally at various follow up assessments (8-12 weeks, 26 weeks or 12-15 months). These effects remained following the adjustment for the influence of covariates. Stamrood et al. 2011 found that the type of HDP (PE or PPROM) did not significantly contribute to developing post-partum PTSD or depression at six weeks or 15 months post-partum. Risk of depression increased with the number of perinatal complications women experienced (Blom et al. 2010), the severity of preeclampsia (mild 23% and severe 44%) (Hoedjes et al. 2011) and preterm birth (Englehard et al. 2002). Risk of PTSD increased with admission to the neonatal intensive care unit, foetal death and history of depression (Hoedjes et al. 2011 and Stamrood et al. 2011). Of the women who had PE and whose babies died in utero, 40% had developed depression and PTSD, compared to 10% in
the women with healthy babies. Previous studies have shown that depressive symptoms and stress prenatally and early in pregnancy have been associated with the development of preeclampsia later in pregnancy (Kurki, Hiilesmaa, Raitasalo, Mattila et al. 2000; Klonoff-Cohen, Cross & Pieper, 1996; Landsbergis & Hatch, 1996). Together these findings suggest that the increased risk of obstetric complications associated with hypertensive disorders of pregnancy contribute towards increased risk of depression and PTSD in the postnatal period.

**Hyperemesis Gravidarum and perinatal mental health.**

The four studies that reviewed the impact of HG found that there was a significant difference in emotional distress in women with HG compared to controls in pregnancy and the postnatal period. Christodoulou-Smith et al. 2011 showed that 18% of women met full diagnostic criteria for PTSD and Senturk et al. 2017 showed a 6.5-fold increased probability of postnatal depression following HG. Women were at increased risk of postnatal mental health difficulties if they were hospitalised in both the 1st and 2nd trimesters (Kjeldgaard et al. 2017) or had a negative birth experience (Kjeldgaard et al. 2018). The overall finding that mental health is negatively affected by HG during pregnancy and may continue even after discontinuation of HG is consistent with the broader research literature on HG (Mitchell-Jones et al. 2017; Meltzer-Brody et al. 2017; Fejzo et al. 2009).

**Pelvic and Lumbar Pain**

Gutke et al. 2007 explored the prevalence of pelvic girdle pain (PGP) and depression postnatally. The authors found that at three months postpartum, 16% of women had PGP, 11% had lumbar pain, and 5% had combined PGP and lumbar pain. The comorbidity of lumbopelvic pain and depressive symptoms was 10%. There was a significant difference in depression for women with lumbar pain or women with PGP compared to controls. These results could be due to women with PGP not being able to perform daily tasks, having reduced
self-efficacy and being hypervigilant to pain, all of which may maintain psychological distress. Indeed Elden et al. 2016 followed up women beyond the perinatal period (<11 years postpartum) and found that compared to women without PGP, women with PGP had significantly increased levels of anxiety and depression.

**Anaemia**

One study found the prevalence of postpartum depression at 4-6 weeks following Anaemia was 5.5% (Goshtasebi, Alizadeh & Gandevani, 2013). If women were anaemic at delivery (<11 g/dL of haemoglobin) it increased the chance of postpartum depression. This is not surprising given that anaemia induces fatigue, so this would exacerbate exhaustion after birth and adjusting to motherhood. However, the findings should be interpreted with caution given the low quality of the study, and that fatigue may be misrepresented as depression. Alharbi and Abdulghani (2014) found that reduction in haemoglobin level is a risk factor for postpartum depression in women and iron supplement as a treatment for postpartum depression has been reported efficacious (Sheikh, Hantoushzadeh, Shariati, Farahani, et al. 2017). Goshtasebi et al. 2013 did not assess whether Anaemia exacerbated pre-existing depression, despite findings of an association between anaemia and depression in the general population (Eizadi-Mood, Ahmadi, Babazadeh, Yaraghi, et al. 2018).

**Discussion**

**Summary of evidence**

Nineteen primary studies met review criteria, which included studies focussed on HG, GDM, HDP, Anaemia and pregnancy-related pelvic/lumbar pain. Across all pregnancy-related illnesses there was evidence of a negative relationship with perinatal mental health difficulties. There was a consistent relationship between HDP and postnatal depression,
Evidence of a relationship between HDP and PTSD in the postnatal period was also consistent, prevalence ranging from 10.5% to 28%. HG was consistently associated with depression and PTSD postnatally, with one study describing PTSD prevalence at 18%. Evidence of a relationship between GDM and antenatal and postnatal depression was inconsistent. Prevalence rates of perinatal depression associated with GDM ranged from 12% antenatally to between 10.3% and 15.1% postnatally. Anaemia was associated with 5.5% of women having depression at 4-6 weeks postnatally. Lumbopelvic pain and postnatal depression had a co-morbid prevalence of 10% at three months postnatally.

To contextualise these findings, it is of note that the prevalence of PTSD associated with HG, HDP and GDM is comparable to the prevalence seen in high-risk perinatal samples. Clinically significant PTSD symptoms have been identified in up to 16.8% of women in community samples following childbirth (Dekel, Stuebe & Dishy, 2017), 3% in low risk groups with no objective threat to life of mother or baby (Grekin & O’Hara, 2014) and 15-18% in high-risk groups, such as women who have experienced severe obstetric complications, preterm birth and caesarean section (Grekin & O'Hara, 2014; Horsch, Brooks, & Fletcher, 2013; Yildiz, et al., 2017).

This systematic review found perinatal death to be a contributing factor to postpartum PTSD and depression. These findings extend the existing data on PTSD and depression following pregnancy loss, stillbirth or perinatal death. Perinatal loss is associated with prevalence of PTSD between 8%-11% between 4-16 months after the loss (Jind, 2003; Horsch, Jacobs & McKenzie-McHarg, 2015) and women who become pregnant after stillbirth have a higher prevalence of anxiety (22.5%) and depression (19.7%) (Gravensteen, Jacobsen et al. 2018). Taken together, perinatal death after pregnancy-related illness contributes to more psychological distress in the perinatal period.

The prevalence of depression associated with GDM, Anaemia or Lumbopelvic pain is slightly less than depression among healthy mothers (without prior history of depression) and
who gave birth to healthy full-term infants, who have a prevalence of depression of 17% (Shorey, Ing, Ng, Huak et al. 2018). The meta-analysis by Shorey et al. (2018) found an increasing incidence beyond six months postnatally, whereas GDM, Anaemia and Lumbopelvic pain studies reviewed in this paper mostly followed up in the early postnatal period, so perhaps the depression rates following these pregnancy-related illnesses were underrepresented.

The prevalence of mental health difficulties associated with all pregnancy-related illnesses reviewed is higher than the general UK population. Local prevalence estimates from The GP Patient Survey identifies that 5.5% of people in the UK have generalised anxiety disorders and 3.3% have depression and 5.1% of women screened positive for PTSD, with the highest prevalence in women aged 16-24 years. However Public Health England notes that these figures may under-represent mental health in the UK population, it is estimated that 50% of patients attending GPs with depressive disorders do not have their symptoms recognised (Baker, 2018).

The relationships between pregnancy-related illnesses and perinatal mental health difficulties were associated with illness factors, prenatal psychological distress and obstetric complications following from pregnancy-related illness such as preterm birth, caesarean section and admission to neonatal intensive care.

**Illness Factors**

A diagnosis of a pregnancy-related illness may be considered as a stressful life event, which itself is an established factor for depression (O’Hara & McCabe, 2013). Women with HG report adverse psychosocial outcomes (Christodoulou-Smith et al. 2011; McCarthy, Khashan, North et al. 2011; Poursharif, Fejzo, Macgibbon et al. 2006) and change to family planning given the potential fear of HG recurrence (Vlachodimitropoulou-Koumoutsea et al. 2013) as the severity of nausea and vomiting of HG is comparable to that of receiving
chemotherapy (Lacroix, Eason & Melzack, 2000). The severity of illness and hospitalisation increased risk of postnatal mental health difficulties in women who experienced HG (Kjeldgaard et al. 2017) and women who experienced pre-eclampsia (Hoedjes et al. 2011). Despite women with GDM or HDP potentially having average glucose and blood pressure levels after delivery, they are at higher risk than unaffected women for developing future chronic disease (Kim, Newton & Knopp, 2002; Sibai, Sarinoglu, & Mercer, 1992). HDP has fewer options for prevention and self-management compared to GDM, so women may be more fatalistic and cynical about their health and feel more depressed.

**Obstetric Factors**

HDP were associated with higher rates of complications than other pregnancy-related illnesses, including higher rates of caesarean birth and preterm delivery (Hedderson, Ferrara & Sacks, 2003; Mackay, Berg & Atrash, 2001), which possibly explains why women with HDP had a higher prevalence of PTSD and depression. If women require an emergency caesarean section, they are more likely to experience physical morbidity in the postnatal period, a well-known stressor because of pain, tiredness and limitations that may contribute to post-partum depression (Xu, Ding, Ma, & Xin, 2017). Preterm complications in women are associated with feelings of helplessness, fear and worry about the health of the baby (Kim et al. 2005). Preterm delivery of infants may result in infants requiring neonatal intensive care unit stays (Blom et al. 2010; Beka et al. 2018), which increases psychological distress.

**Prenatal psychological distress**

This systematic review found that a history of psychological distress can impact the adjustment and coping with a diagnosis of pregnancy-related illness. Prenatal depressive symptoms may have impacted coping with a diagnosis of GDM (Bryn & Penckofer, 2015). PTSD symptoms following HDP were more strongly associated with psychological factors than
with objective indicators of condition-severity (Engelhard et al. 2002; Bowman, 1999; Stramrood et al. 2011). Psychological distress following HG was associated with antenatal anxiety and depression (Senturk et al., 2017) and prenatal PTSD, depression and adverse life events (Kjeldgaard et al. 2018). Sociodemographic factors significantly associated with postnatal mental health difficulties following HG were higher BMI, younger age, shorter education and lower socio-economic status, consistent with other research on HG (Roseboom, Ravelli, van der Post, & Painter, 2011; Chou, Kuo & Wang, 2008). These factors may have increased vulnerability to mental health difficulties (Grekin & O’Hara, 2014). Consistent with the findings of this review, a recent meta-analysis highlighted current depression, poor interpersonal relationships with medical professionals, low social support, and a pre-pregnancy history of adversity and psychopathology as risk factors for postnatal PTSD and depression (Furtado et al. 2018).

Physiological mechanisms mediating the relationship between pregnancy-related illnesses and perinatal mental health

Hormonal and physical changes may mediate the association between pregnancy-related illnesses and perinatal mental health. Women with pre-eclampsia have increased serotonin levels in the blood so one theory is that there may be decreased levels of serotonin in the brain, contributing to depressive symptoms (Bolte, van Geijn & Dekker, 2001; Bloch, Schmidt, Danaceau et al. 2000). Abnormal glucose metabolism in GDM might partially induce dysregulation of the hypothalamic–pituitary–adrenal axis and increase cytokine-mediated inflammatory responses, which are associated with decreased serotonin production and depression (Moulton, Pickup & Ismail, 2015). The altered metabolic state related to GDM could further impact neurological functions or hormonal changes that occur postpartum, potentially increasing the risk of depression (Sandu, Buga, Uzoni et al. 2017). For example, increased inflammation is associated with an increased risk of atypical depression, possibly
the subtype of depression more commonly seen in the postnatal period (Lamers, Vogelzangs & Merikangas, 2013; Kammerer, Taylor & Glover, 2006).

**Implications for clinical practice**

High-quality clinical care, information, and support may help ameliorate the psychological impact of pregnancy-related illnesses (Leeners, Rath, Kuse, Neises et al. 2006). Current options for treatment for pregnancy-related illnesses are mainly restricted to symptom relief. For example, for HG, this includes such as anti-emetics, rehydration and supplementation of vitamins and nutrients (Grooten, Roseboom & Painter, 2015). Healthcare professionals could intervene with psychologically informed treatment plans to alleviate reactive anxiety and to prevent a sense of helplessness and fear, which may lead to symptoms of PTSD. A well-communicated treatment plan and educational training motivate pregnant women with GDM and helps them feel secure for themselves and their baby (Langer & Langer, 1994; Daniels et al. 2003). An advanced treatment plan for ‘preterm’ complications will help women to gather information for decision making as recommended by the World Health Organisation (WHO, 2001) and to get more security and empowerment.

Unresolved PTSD, anxiety and depression symptoms may persist for several years after the incident pregnancy, are predictive of adverse obstetric and neonatal outcomes (Chung, Lau, Yip, Chiu et al. 2001) and may severely affect women’s health and psychosocial wellbeing. A cognitive behaviour conceptualisation would suggest that women with PTSD may avoid a future pregnancy for fear of it reactivating cues reminiscent of aspects of pregnancy-related illness (Foa, Steketee & Rothbaum, 1989). PTSD and depression influence maternal-infant attachment and infant development (Yarcheski, Mahon, Yarcheski et al. 2009). Antenatal depressive symptoms are the strongest predictor of postnatal depression (Robertson, Grace, Wallington & Stewart, 2004) which can adversely affect the emotional, behavioural, and cognitive development of the offspring (Murray & Cooper, 1997).
Screening for depressive symptoms, anxiety and PTSD in antenatal appointments is essential to identify women at risk. Women who are depressed often do not seek help on their own, or they consult with people who are not professional healthcare providers (Eilat-Tsanani, Merom, Romano, Reshef et al. 2006) so it is essential that obstetricians, midwives, general practitioners, and staff at baby clinics are aware of the substantially increased risk of psychological distress associated with pregnancy-related illness. These staffs are in a central position to prevent adverse consequences and provide support and referral to clinical psychology for trauma focussed psychological intervention (Furata, Horsch, Ng, Bick et al. 2018).

Rapid recognition and referral are associated with shorter treatment duration and improves the function of the mother (Poel et al. 2009) which in turn has a beneficial effect on infant development (Kingston, Tough, & Whitfield, 2012) and family functioning (Cluxton-Keller & Bruce, 2018). National Institute for Clinical Excellence guidelines (NICE, 2015) on antenatal and postnatal mental health recommend that mothers who have PTSD are offered Eye Movement Desensitisation and Reprocessing Therapy (EMDR) or trauma-focused Cognitive Behaviour Therapy. However, despite the guidance and policy drivers advocating for perinatal mental health services, the provision of these services is patchy (Bauer et al., 2014). Improvements are needed to develop consistent organizational service structures to facilitate integrated care pathways and to standardize the mental health training for staff supporting women in the perinatal period.

**Future research**

Future prospective studies reviewing associations between pregnancy-related illness and perinatal mental health would benefit from controlling for potential confounders such as a history of trauma and psychological distress, measures of parent-baby bonding and social support. These potential risk and protective factors will be better evaluated when outcomes are measured at regular fixed time-points. There is a need to elucidate the shared
pathophysiology of pregnancy-related illness and perinatal mental health to assess how endocrine and immunological factors could mediate the relationship. A review of optimal psychological support in the perinatal period for women who have experienced pregnancy-related illness is needed. These findings can be used to guide the expectations of women and their providers.

**Strengths**

This is the first systematic review to address the impact of pregnancy-related illnesses, specifically GDM, HDP, HG, Anaemia and lumbar/pelvic pain, on perinatal mental health. Most studies were prospective and adjusted for covariates in the analyses, so it was possible to assess the temporal impact of pregnancy-related and risk factors for perinatal distress. Despite the range of sample sizes across studies and the variance in participants socio-economic status and education level, most studies were of high quality and presented data comparing characteristics of respondents and non-respondents thereby reducing risk of bias for study participation and attrition.

**Limitations**

The comparability of studies is reduced due to different comparison groups, outcomes (occurrence and severity) and a range of questionnaires to assess anxiety, PTSD and depression. Questionnaires relied on self-report to determine mental health difficulties so that response bias may have been present. There is limited literature concerning the optimal choice of measurement instruments for psychological distress in perinatal settings, and different measures have varying validity and reliability (Nast, Bolton et al. 2013). The different timings of assessment and lengths of follow-up mean it is difficult to establish whether changes in perinatal psychological distress is linear. Several pregnancy-related illnesses in the search criteria are not included in this review due to a lack of literature examining the psychological impact or restricted to qualitative studies (Dekker, Morton, Singleton & Lyndon 2016).
Conclusion

Women who experience pregnancy-related illnesses are at increased risk for anxiety, depression and PTSD in the perinatal period. These relationships are often associated with prenatal psychological distress, illness factors and associated obstetric complications. The association of pregnancy-related illness with psychological distress, signifies the need for monitoring mental health throughout pregnancy and postnatally and for health-care services to intervene as recommended by current guidelines (NICE, 2015).

Acknowledgements

The authors would like to acknowledge the helpful advice and support of clinicians working in XXXX perinatal mental health team. The authors would also like to extend special thanks to the women who shared their experiences of the psychological impact of pregnancy-related illness that influenced the design of this systematic review.

Declaration of interest

The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper. The research was conducted as part of a Clinical Psychology Doctorate programme.


Paper Two: Empirical Study

Testing a cognitive model to predict posttraumatic stress disorder in women following experiences of Hyperemesis Gravidarum

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Paper two has been prepared for submission to British Journal of Clinical Psychology (see Appendix 5 for submission guidelines).

For ease of reading, tables have been included in the text rather than in appendices.

Word Count = 4999 (excluding tables, figures and references)
Abstract

**Background:** Hyperemesis Gravidarum (HG) is a pregnancy illness characterised by extreme persistent nausea and vomiting that affects 0.3-2% of women and has significant negative consequences for maternal psychosocial wellbeing including posttraumatic stress disorder (PTSD). Ehlers and Clark cognitive model of PTSD applies to a range of trauma samples but has not been studied in the context of HG. This study investigated whether theoretically derived variables of the cognitive model explained unique variance in postnatal PTSD symptoms when key sociodemographic, HG variables and potential protective factors of dispositional mindfulness, general self-efficacy and postnatal social support were controlled.

**Method:** This study used a retrospective cross-sectional design. Two hundred sixty-six women who had experienced HG completed validated questionnaires in an online survey assessing PTSD, dysfunctional cognitive appraisals and responses to intrusions, sociodemographic and HG variables and potential protective factors.

**Results:** The PCL5 PTSD screening questionnaire suggested that 40.6% of the sample experienced trauma symptoms. Sociodemographic and HG variables alone did not significantly predict variance in PTSD symptoms; protective factors alone predicted 31.2% variance and cognitive behavioural predictors alone predicted 62.3%. The final hierarchical regression model identified that negative cognitions about the self predicted 10% of PTSD symptoms and responses to intrusions (suppression, rumination and numbing) predicted 52.2%.

**Conclusions:** Key elements of Ehlers and Clark’s (2000) cognitive model, negative cognitions about the self and responses to intrusions, significantly predict variance in PTSD symptoms following HG, when sociodemographic, HG variables and protective factors are controlled.
Keywords
Hyperemesis Gravidarum, Postnatal, Cognitive model, Traumatic, PTSD, Dispositional Mindfulness, General self-efficacy, Postnatal social support, Cognitive Behaviour Therapy

Practitioner Points

- Ehlers and Clark’s (2000) cognitive model has utility for formulating and informing the psychological intervention for PTSD following HG.

- The strongest predictors of PTSD symptoms following HG were negative cognitions about the self, suppression, numbing and rumination. Therefore, these variables would be most valuable to identify and target.

- Future research should investigate the efficacy of Cognitive Behaviour Therapy for PTSD in the context of Hyperemesis Gravidarum.

Statement of contribution

What is already known on this subject?
HG is associated with negative psychosocial outcomes and increased risk of psychological distress in pregnancy and the postnatal period.

What does this study add?
This is the first study to test the validity of the cognitive model of PTSD for women with a history of HG and the results highlight the strength of the cognitive behavioural variables in predicting PTSD symptoms. This study highlighted that risk factors associated with PTSD symptoms were young age, low socio-economic status and being single. High dispositional mindfulness, high general self-efficacy and good postnatal social support are protective factors against PTSD symptom severity.
**Background**

Hyperemesis gravidarum (HG) is a pregnancy condition characterised by persistent and excessive vomiting, dehydration, ketonuria, fatigue, metabolic disturbances and nutritional deficiencies which can lead to hospitalisation (Kjeldgaard, Vikanes, Benth, Jung et al. 2018; RCOG, 2016). The reported incidence of 0.3–2% varies across ethnic groups and is dependent on diagnostic criteria (Einarson, Piwko & Koren, 2013) and it is estimated that 30% of pregnant women do not receive a diagnosis of HG despite high levels of nausea and vomiting (Gadsby & Barnie-Adshead, 2011). HG is the most common reason for admission to hospital in the first half of pregnancy and is second only to preterm labour as a cause of hospitalisation during pregnancy (Hod, Orvieto, Kaplan, Friedman et al. 1994; McCarthy, Khashan, North, Moss et al. 2011). Some women who experience HG may have an increased risk of preterm birth and babies with low birth weight (Veenendaal, van Abeelen, Painter, van der Post et al. 2011).

The aetiology of HG is likely to be multifactorial with research demonstrating hormonal risk factors (Grooton, Roseboom & Painter, 2015), genetic risk factors (Fejzo, Sazonova, Sathirapongsasuti et al. 2018) and a strong influence of maternal genes with heritability estimates up to 73% (Colodro-Conde, Jern, Johansson et al. 2016). HG has a history of stigmatisation due to a misguided theory of psychiatric aetiology (Fejzo & MacGibbon, 2012). Women who experience prenatal psychological distress may find it harder to adjust to HG, and their psychological distress is exacerbated in the context of the physical condition of HG (Mitchell-Jones, Gallos, Farren, Tobias et al. 2017; Kjeldgaard, Eberhand-Gran, Benth et al. 2017).

HG is associated with adverse psychosocial outcomes, including difficulties with breastfeeding, low self-esteem, social isolation, marital problems and loss of employment (McCarthy et al. 2011; Poursharif, Korst, Fejzo, MacGibbon et al. 2008; Dean, Bannigan & Marsden, 2018; Chou, Avant, Kuo & Fetzer, 2008). Women may be fearful of becoming pregnant again following HG and opt for elective termination of subsequent unplanned
pregnancy (Poursharif et al. 2008; Dean et al. 2018). Health professionals, social workers, and the general public often underestimate the adverse impact of HG on womens lives (Sykes, Swallow, Gadsby, Barnie-Adshead et al. 2013; Dean & Marsden, 2017). Women who report that their healthcare provider was uncaring or unaware of the severity of their symptoms are almost twice as likely to report adverse psychological sequelae (Poursharif et al. 2008).

Depression, anxiety, PTSD and maternal–foetal attachment have been studied in relation to HG (Mitchell-Jones et al. 2017; Kjeldgaard et al. 2018; McCormack, Scott-Heyes, McCusker; 2011). Women with HG experience higher levels of depression and anxiety compared to women without HG (Kjeldgaard et al. 2017; Mitchell-Jones et al. 2017; Yildiz, Ayers & Phillips, 2017). There is an increased risk of PTSD associated with HG, particularly for women with persistent HG (Christodoulou-Smith, Gold, Romero, Goodwin et al. 2011; Meltzer-Brody, Maegbaek, Medland et al. 2017; Fejzo, Poursharif, Korst, Munch et al. 2009; Mullin, Ching, Schoenberg, MacGibbon et al. 2012) and PTSD symptoms are maintained two years later (Kjeldgaard et al. 2018). PTSD is highly distressing for the mother and can negatively impact the couple relationship (Nicholls & Ayers, 2007), mother-infant relationship (Ionio & Di Blasio, 2014), and infant’s behaviour and cognitive development (Cook, Ayers & Horsch, 2018). Furthermore, PTSD during a subsequent pregnancy is associated with having an infant of lower birth weight (Yonkers, Smith, Forray, Epperson et al. 2014), preterm delivery and increased rates of elective caesarean sections (Khashan, McNamee, Abel, Mortensen et al. 2008). A better understanding of the risk and protective factors for developing PTSD in the context of HG is required to reduce the adverse psychological sequelae through improved early detection and intervention strategies.

There is a limited understanding of the psychological processes that maintain the traumatic stress response in the context of HG. Intervening at the level of cognitive processes offers one opportunity to mitigate against the maintenance and/or exacerbation of PTSD symptoms associated with a HG pregnancy. Ehlers and Clark (2000) cognitive model of PTSD is often used in clinical psychology practice to devise psychological formulation and CBT
intervention for adults with PTSD. Ehlers and Clark suggest that a sense of current threat is produced by negative cognitive appraisals of the trauma and/or its sequelae coupled with a fragmented and poorly integrated memory of the trauma. This threat can be unintentionally triggered by a range of stimuli and situations reminiscent of the traumatic experience/s. The perception of current threat is accompanied by symptoms of intrusions, arousal and negative emotions (e.g. anxiety, anger, depression). PTSD is maintained by appraisals that motivate unhelpful cognitive (e.g. rumination) and behavioural (e.g. avoidance) strategies. These strategies have the paradoxical effect of maintaining PTSD symptoms as they prevent a cognitive change of negative appraisals of the trauma and sequelae. Also, the trauma memory is prevented from being elaborated, contextualised and integrated into autobiographical memory. The model components have robust support in the general PTSD literature (Ehlers, Ehring & Kleim, 2012).

The applicability of the cognitive model to the HG population needs considering given the qualitative difference between the experience of HG and what is traditionally considered a traumatic experience. HG is a persistent threatening illness that may cause a woman to feel debilitated and terrified that her and/or her baby’s life is in danger and some women consider termination (Dean & Murphy, 2015). Furthermore, anxiety related to medication to control HG symptoms, the stigma surrounding HG, and feelings of helplessness and hopelessness; may serve to predict the onset and maintenance of PTSD symptoms long after pregnancy (McCormack et al. 2011; Dean, 2016).

It is also essential to explore the factors that may protect against the development of PTSD in the HG population. There is evidence to suggest that general self-efficacy (GSE), social support and dispositional mindfulness may protect against perinatal mental health problems (Hall, Beattie, Lau, East et al. 2016). Theoretical models explaining posttraumatic adaptation specify that GSE and resources of social support may be necessary for posttraumatic recovery (Benight & Bandura, 2004). GSE plays a key role in stress reactions and quality of coping in threatening situations (Bandura, 1997). This psychological construct is positively associated
with optimism, self-regulation, stress-appraisal and self-esteem and negatively associated with depression and anxiety (Luszczynska, Gutiérrez-Doña, & Schwarzer, 2005; Cieslak, Benight, Schmidt, Luszczynska, et al. 2009). GSE has also been shown to be negatively correlated with intrusion, hyperarousal, and traumatic stress symptoms and positively correlated with posttraumatic growth (Mystakidou, Parpa, Tsilika, Panagiotou et al. 2015). There is an evolving and promising evidence base showing the effectiveness of mindfulness to promote perinatal mental health and to target processes that maintain PTSD (Lang, 2017). Specifically, the mindfulness practice of present moment, focused non-judgemental attention can reduce physiological arousal, increase attentional control and foster acceptance of unwanted experiences (Lang, Strauss, Bomyeea et al. 2012).

Previous research has tested a cognitive model of PTSD following childbirth (King, McKenzie-McHarg & Horsch, 2017). A similar methodology was adapted for the present study in order to test a cognitive model of PTSD following HG. The present study will investigate whether variables of the Ehlers and Clark cognitive model explain unique variance in postnatal PTSD symptoms, this will be analysed when key sociodemographic, HG variables and protective factors are controlled.

**Hypotheses**

1. Sociodemographic and HG variables will explain small variance in PTSD symptoms;
2. Cognitive appraisals and responses to intrusions will explain medium variance in PTSD symptoms;
3. Higher scores of dispositional mindfulness, social support and general self-efficacy will be associated with less severe PTSD symptoms; and
4. Cognitive appraisals and responses to intrusions will explain additional unique variance in PTSD symptoms when sociodemographic, HG variables and protective factors are controlled.
Method

Women over the age of 18, English speaking, and had experienced HG were eligible to participate. As there is no widely accepted point for which nausea and vomiting in pregnancy becomes HG, all women who have experienced severe vomiting and nausea and who received ‘second level intervention’ were eligible (Painter, Boelig, Kelly & Grooten, 2015). Second level intervention is defined by O’Donnell et al. 2016 as when a woman presents to medical care (a GP in primary care and/or outpatient/inpatient treatment from a general hospital/maternity unit). All women who met these inclusion criteria regardless of the length of time since a HG pregnancy were eligible to participate. In total, 656 women accessed the online survey which contained several arms of research. Of relevance to the present study, 266 women had complete data sets.

Procedure

Data was collected using an online survey, advertised by Pregnancy Sickness Support Website from October 2018 through January 2019. Pregnancy Sickness Support (PSS) is a charity that supports women with HG and their families to cope physically, mentally and emotionally. Qualtrics survey software (Snow and Mann, 2013) allowed women to participate anonymously online, through Cardiff University. The link to the password protected survey was shared by Pregnancy Sickness Support using social media.

Measures

Posttraumatic stress disorder symptoms

Posttraumatic stress disorder checklist for DSM-5 (PCL5; Blevins, Weathers, Davis, Witte et al. 2015). The PTSD Checklist for DSM-5 (PCL-5) is a 20-item self-report measure that assesses the presence and severity of PTSD symptoms. The PCL-5 can be used to screen individuals for PTSD (cut-point of 33) and to monitor changes in symptom severity. The PCL-5 has good psychometric properties (Boivin, Marx, Weathers, Gallagher et al. 2016; Wortman, Jordan, Weathers, Resick et al. 2016). For the current study, Cronbach’s alpha reliability coefficients
for the subscales were .780 (intrusion) .833 (avoidance and numbing), .768 (arousal and reactivity), .731 (cognition and mood) and .838 for the total.

**Cognitive and Behavioural Predictors of PTSD**

**Negative appraisals of trauma and/or its sequelae**

**The Posttraumatic Cognitions Inventory (PTCI; Foa & Ehlers, 1999)**

PTCI is a 33-item measure of trauma-related thoughts and beliefs. The PTCI assesses three features of traumatic thoughts: negative cognitions about the self, negative cognitions about the world and self-blame. The PTCI has adequate psychometric properties in the postnatal population (Ford, Ayers & Bradley, 2010). For the current study, Cronbach’s alpha reliability coefficients for the subscales were .638 (negative cognitions about the self), .823 (negative cognitions about the world), .860 (self-blame), and .765 for the total.

**Dysfunctional cognitive and behavioural strategies**

**The Response to Intrusions Questionnaire (RIQ; Steil & Ehlers, 2000).**

The RIQ is a 19-item inventory that assesses how women use unhelpful cognitive and behavioural strategies when experiencing intrusions of the trauma. The RIQ is suitable for use in a perinatal population (Clohessy & Ehlers, 1999). It contains three subscales: efforts to suppress thoughts and intrusions, rumination, and numbing of memories (detaching/dissociation). For the current study, Cronbach’s alpha reliability coefficients for the subscales were .655 (rumination), .854 (suppression), .854 (numbing/dissociation), and .649 for the total.

**Sociodemographic and HG clinical factors**

The research literature informed the choice of sociodemographic and HG variables assessed in this study (Grekin & O’Hara, 2014; Christodoulou-Smith et al. 2011; Kjeldgaard et al. 2018). Sociodemographic variables included: education, ethnicity, household income, and marital status. HG factors included: age, time since HG pregnancy, number of times hospitalised for HG and number of times experienced HG. If women had more than one pregnancy affected
by HG, they were asked to respond to each questionnaire considering their worst experience of HG pregnancy.

**Potential protective factors for PTSD severity**

**Postnatal social support**

The Medical Outcomes Study Social Support Survey (MOSSSS; Sherbourne & Stewart, 1991)

The MOSSSS measures four aspects of social support: emotional/informational, tangible, affectionate and positive social interaction. All subscales have good reliability, are stable over time and show fair construct validity (Sherbourne & Stewart, 1991). For the current study, Cronbach’s alpha reliability coefficients for the subscales were .723 (emotional/informational support), .792 (tangible support), .823 (affectionate support), .792 (positive social interaction) and .861 for the total.

**Mindfulness**

Five Factor Mindfulness Questionnaire (FFMQ; Baer, Smith, Hopkins, Krietemeyer et al. 2006)

The five facets of mindfulness are observing, describing, acting with awareness, non-judging of inner experience, and non-reactivity to inner experience. The 24-item short form of the FFMQ (FFMQ-SF) has good psychometric properties, is highly sensitive to change and has been validated in the perinatal population (Taylor, Cavanagh & Strauss, 2016). For the current study, Cronbach’s alpha reliability coefficients for the subscales were .780 (observing), .721 (describing), .730 (acting with awareness), .735 (non-judging of inner experience), .749 (non-reactivity to inner experience) and .738 for the total.

**General Self-efficacy**

The General Self-Efficacy Scale (GSE; Schwarzer & Jerusalem, 1995)

For the GSE, the total score ranges between 10 and 40, with a higher score indicating more self-efficacy. The GSE has good internal reliability, is positively correlated to optimism and negatively correlated to depression, stress, health complaints and anxiety. For the current study, Cronbach’s alpha reliability coefficient for the total score was .933.
Data Analysis

Data was analysed by IBM SPSS Statistics 20 and initially descriptive statistics were used to describe the sample. All continuous variables were assessed for violations of normality using skewness and kurtosis statistics. For dichotomous variables, the distribution of the dependent variable (PTSD symptom severity measured by PCL5 total score) was assessed across each independent variable. As the PCL5 total score violated the assumption of normality, Spearman’s Rho correlations were used to assess the relationships between all continuous independent variables and the dependent variable. Ordinal variables of education, income level, number of times experienced HG and number of times admitted to hospital were analysed by Kendall’s Tau. Nominal categorical variables of ethnicity and marital status were analysed by eta.

Simultaneous regression was used to answer the first, second and third hypotheses. Hierarchical regression was used to test the fourth hypothesis. Assumptions of normally distributed residuals were met for regression analyses so it was acceptable for variables that were not normally distributed to be included. All regression analyses also met assumptions regarding the linearity of relationships, absence of collinearity, and independence of errors. Visual inspection of a matrix scatterplot showed no evidence of heteroscedasticity (Laerd, 2015).

Only those variables that had a significant relationship with the PCL5 total score were included in subsequent regression analyses. Total scores of mindfulness, general self-efficacy and postnatal social support were inputted into hierarchical regression considering the homogeneity and multicollinearity of the subscales, as identified by inspection of Cronbach’s alpha reliability coefficients. Only those variables that significantly predicted variance in PCL5 total score in logistic and simultaneous regression analyses were included in the final hierarchical regression analysis. Hierarchical regression was conducted to investigate whether posttraumatic cognitions and response to intrusions explained more variance in PTSD symptom severity than the variance predicted by mindfulness. A priori power
calculation assuming a medium effect size of 0.15, \( \alpha \) error probability = .05 and power (\( \alpha - \beta \) err prob) = .80 was used was to guide participant recruitment of n =258.

**Results**

Two hundred sixty-six women had complete data sets for all items on sociodemographic variables, HG variables, questionnaires that assessed the cognitive behavioural model for PTSD and potential protective variables. In summary, the sample were predominately British or Irish (84%) females with a mean age of 27 years (SD=5.47), married (70.7%) with a range of highest education level (11.7% GCSE to 66.2% at degree or postgraduate level) and slightly above average household income based on UK national norms according to the Office for National Statistics (mean income £48,924, SD=24,367) (ONS, 2018). Most women accessed professional support via their GP or midwife or online. The mean time since HG pregnancy was 22 months (range 0-100 months) and the mean number of times hospitalised for HG was 2.73 times (range 0-10). 38% of women experienced HG once, 36% twice, 12% three times and 14% four times or more.

**Symptoms of PTSD associated with a HG pregnancy**

The mean total PCL5 score was 29.74 (SD=17.51); 40.6% of women scored more than 33 points which is a cut-off typically used to indicate that women may be experiencing PTSD and would warrant full assessment by clinical interview. The mean PTCI score was 100.44 (SD=44.56); 26.3% of women scored a total score of more than 133, suggesting these women had trauma-related thoughts in the range of those who have PTSD (Foa et al. 1991) (see Table 1).
Table 1: Cognitive behavioural data of the sample

<table>
<thead>
<tr>
<th>Questionnaires</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCL5 Total</td>
<td>29.74 (17.51)</td>
</tr>
<tr>
<td>PTCI Total</td>
<td>100.44 (44.56)</td>
</tr>
<tr>
<td>PTCI subscales:</td>
<td></td>
</tr>
<tr>
<td>Negative cognitions about self</td>
<td>62.93 (28.43)</td>
</tr>
<tr>
<td>Mean score per statement for subscale</td>
<td>2.99 (1.35)</td>
</tr>
<tr>
<td>Negative cognitions about world</td>
<td>22.87 (10.67)</td>
</tr>
<tr>
<td>Mean score per statement for subscale</td>
<td>3.26 (1.52)</td>
</tr>
<tr>
<td>Self-blame</td>
<td>14.63 (7.14)</td>
</tr>
<tr>
<td>Mean score per statement for subscale</td>
<td>2.92 (1.42)</td>
</tr>
<tr>
<td>RIQ Total</td>
<td>46.06 (11.86)</td>
</tr>
<tr>
<td>RIQ subscales:</td>
<td></td>
</tr>
<tr>
<td>Suppression</td>
<td>16.72 (4.78)</td>
</tr>
<tr>
<td>Rumination</td>
<td>21.06 (7.25)</td>
</tr>
<tr>
<td>Numbing/Dissociation</td>
<td>5.26 (2.08)</td>
</tr>
</tbody>
</table>

SD standard deviation, PCL5 PTSD Checklist for DSM-5, PTCI Posttraumatic Cognitions Inventory, RIQ Response to Intrusions Questionnaire

To contextualise these results, comparisons were made between the PCL5 scores for women who had experienced HG against a clinical sample (military veterans) and a non-clinical sample (students) (see Table 2). The PCL-5 has shown validity, reliability and sensitivity to change over time in military service members and undergraduate students who had experienced stressful life event/s (Wortman et al. 2016; Blevins et al. 2015).

Table 2: A comparison of mean and standard deviation scores on the PCL5 measure in non-clinical sample, HG sample and clinical sample.

<table>
<thead>
<tr>
<th></th>
<th>Students</th>
<th>HG</th>
<th>Military Veterans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample Size</td>
<td>262</td>
<td>266</td>
<td>92</td>
</tr>
<tr>
<td>Mean</td>
<td>15.42</td>
<td>29.74</td>
<td>42.41</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>14.72</td>
<td>17.51</td>
<td>15.06</td>
</tr>
</tbody>
</table>

An independent samples t-test was conducted to compare PCL5 mean scores between samples. There was a significant difference between HG and students, t (265) =13.336, p<0.05 and between HG and military veterans, t (265) =11.798, p<0.05. This suggests that the HG
group may experience trauma symptoms to a different severity compared to non-clinical and clinical samples.

The PTCI compares favourably with other measures of trauma-related cognitions, especially in its superior ability to discriminate between traumatised individuals with and without PTSD (Foa et al. 1999). Table 3 compares the median scores on each subscale of the PTCI for people who have experienced HG and people traumatised with and without PTSD. Considering the median scores and standard deviations it is apparent that some people with HG experience it as traumatic, similarly to people who have experienced traumas such as disasters/accidents, nonsexual assault, sexual assault, and life-threatening illness (Foa et al. 1999).

Table 3: A comparison of median and standard deviation scores on the PCTI measure in HG sample compared to people who have experienced trauma and a control group of no trauma

<table>
<thead>
<tr>
<th></th>
<th>No trauma ‡¹</th>
<th>Trauma but no PTSD ‡</th>
<th>Hyperemesis Gravidarum ‡²</th>
<th>Trauma and PTSD ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTCI</td>
<td>Median</td>
<td>SD</td>
<td>Median</td>
<td>SD</td>
</tr>
<tr>
<td>Total</td>
<td>45.5</td>
<td>34.76</td>
<td>49</td>
<td>23.52</td>
</tr>
<tr>
<td>Negative cognitions about the self</td>
<td>1.08</td>
<td>0.76</td>
<td>1.05</td>
<td>0.63</td>
</tr>
<tr>
<td>Negative cognitions about the world</td>
<td>2.07</td>
<td>1.43</td>
<td>2.43</td>
<td>1.42</td>
</tr>
<tr>
<td>Self-blame</td>
<td>1</td>
<td>1.45</td>
<td>1</td>
<td>1.02</td>
</tr>
</tbody>
</table>

SD Standard Deviation

Association between sociodemographic, HG clinical factors, cognitive, behavioural and protective factors with PTSD symptoms.

Due to violation of the assumption of normality on the Kolmogorov-Smirnov test for PCL5 scores, non-parametric correlation tests were conducted to identify whether sociodemographic, HG variables, cognitive (PTCI), behavioural (RIQ), mindfulness (FFMQ)

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¹ ‡ Data from Foa et al. 1999
² † Data collected in this study
postnatal social support (MOSSSS) and general self-efficacy (GSE) variables were associated with PTSD symptom severity (PCL5 total score) (Table 4). Income level and age were significantly negatively correlated with PCL5 score. Marital status (single) was significantly positively correlated with PCL5 score. Length of time since HG pregnancy and number of times hospitalised for HG were negatively correlated with PCL5 score but not significantly. All subscales of the cognitive (PTCI) and behavioural (RIQ) variables were significantly positively correlated with PCL5 score. The significant negative correlations between MOSSSS total score and all four subscales, FFMQ total score and majority of subscales (except for observing) and GSE total score suggests that high social support, high dispositional mindfulness and high self-efficacy are protective factors against PTSD symptom severity.
Table 4: A correlation matrix to show the relationship between PTSD severity and sociodemographic, HG clinical, cognitive, behavioural, and confounding variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sociodemographic</strong></td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td>.009 ‡</td>
</tr>
<tr>
<td>Income level</td>
<td>-.146** †</td>
</tr>
<tr>
<td>Education</td>
<td>-.088 †</td>
</tr>
<tr>
<td>Marital status</td>
<td>.141* ‡</td>
</tr>
<tr>
<td><strong>HG clinical variables</strong></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-.233**</td>
</tr>
<tr>
<td>Length of time since HG pregnancy</td>
<td>-.037</td>
</tr>
<tr>
<td>Number of times hospitalised for HG</td>
<td>-.031 †</td>
</tr>
<tr>
<td>Number of times experienced HG</td>
<td>.074 †</td>
</tr>
<tr>
<td><strong>Cognitive variables</strong></td>
<td></td>
</tr>
<tr>
<td>Posttraumatic Cognitions Inventory (PTCI)</td>
<td>.738**</td>
</tr>
<tr>
<td>Negative cognitions about the self</td>
<td>.727**</td>
</tr>
<tr>
<td>Negative cognitions about the world</td>
<td>.678**</td>
</tr>
<tr>
<td>Self-blame</td>
<td>.699**</td>
</tr>
<tr>
<td><strong>Behavioural Variables</strong></td>
<td></td>
</tr>
<tr>
<td>Response to Intrusions Questionnaire (RIQ)</td>
<td>.706**</td>
</tr>
<tr>
<td>Suppression</td>
<td>.485**</td>
</tr>
<tr>
<td>Rumination</td>
<td>.676**</td>
</tr>
<tr>
<td>Numbing</td>
<td>.550**</td>
</tr>
<tr>
<td><strong>Confounding variables</strong></td>
<td></td>
</tr>
<tr>
<td>Mindfulness FFMQ Total score</td>
<td>-.534**</td>
</tr>
<tr>
<td>Observing</td>
<td>-.092</td>
</tr>
<tr>
<td>Describing</td>
<td>-.397**</td>
</tr>
<tr>
<td>Acting with awareness</td>
<td>-.470**</td>
</tr>
<tr>
<td>Non-judging of inner experience</td>
<td>-.505**</td>
</tr>
<tr>
<td>Non-reactivity to inner experience</td>
<td>-.357**</td>
</tr>
<tr>
<td>Social support MOSSSS Total score</td>
<td>-.323**</td>
</tr>
<tr>
<td>Emotional/informational</td>
<td>-.348**</td>
</tr>
<tr>
<td>Tangible</td>
<td>-.205**</td>
</tr>
<tr>
<td>Affectionate</td>
<td>-.206**</td>
</tr>
<tr>
<td>Positive social interaction</td>
<td>-.293**</td>
</tr>
<tr>
<td>General self-efficacy GSE</td>
<td>-.339**</td>
</tr>
</tbody>
</table>

Rs Spearman’s Rho correlation coefficient, *p<0.05 ** p <.01. † Kendall’s τb correlation coefficient, ‡eta correlation
A logistic regression analysis was used to analyse whether sociodemographic and HG clinical variables predicted a significant amount of the variance in PCL5 score. Only variables that had a significant relationship with the PCL5 score (see Table 4) were inputted (n=3). None of these variables statistically significantly predicted PTSD symptom severity. Regression coefficients and standard errors can be found in Table 5.

A linear regression analysis was used to analyse whether cognitive behavioural variables predicted a significant amount of the variance in PCL5 score. Only variables that had a significant relationship with the PCL5 score (see Table 4) were inputted (n=6). These variables statistically significantly predicted 62.3% PTSD symptom severity $F(6, 259) = 73.969$, $P<0.0005$, adj. $R^2=.623$, a medium size effect, according to Cohen (1988). Negative cognitions about the self and all RIQ subscales were significant predictors of PTSD symptom severity ($p<0.0005$) (see Table 5).

A linear regression analysis was used to analyse whether protective variables (GSE, MOSS and FFMQ) predicted a significant amount of the variance in PCL5 score. Protective variables statistically significantly predicted 31.2% PTSD symptom severity $F(3, 262) = 39.664$, $P<0.0005$, adj. $R^2=.304$, a small size effect, according to Cohen (1988). Only the FFMQ total score was a significant predictor of PTSD symptom severity ($p<0.0005$) (see Table 5).
Table 5: A regression matrix to show the various predictors of PTSD symptom severity.

<table>
<thead>
<tr>
<th>Variable</th>
<th>β</th>
<th>SE</th>
<th>t</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sociodemographic and HG clinical variables</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Constant)</td>
<td>1.841</td>
<td>.735</td>
<td>6.281‡</td>
<td>.012</td>
</tr>
<tr>
<td>Household income</td>
<td>-.006</td>
<td>.006</td>
<td>.942‡</td>
<td>.332</td>
</tr>
<tr>
<td>Marital Status</td>
<td>-.671</td>
<td>.473</td>
<td>2.016‡</td>
<td>.156</td>
</tr>
<tr>
<td>Age</td>
<td>-.050</td>
<td>.026</td>
<td>3.536‡</td>
<td>.060</td>
</tr>
<tr>
<td>Cognitive Model</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Constant) for CBT model</td>
<td>-13.218</td>
<td>2.604</td>
<td>-5.077</td>
<td>.000*</td>
</tr>
<tr>
<td>Posttraumatic Cognitions Inventory (PTCI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative cognitions about the self</td>
<td>.146</td>
<td>.062</td>
<td>2.378</td>
<td>.018*</td>
</tr>
<tr>
<td>Negative cognitions about the world</td>
<td>.189</td>
<td>.127</td>
<td>1.491</td>
<td>.137</td>
</tr>
<tr>
<td>Self-blame</td>
<td>.400</td>
<td>.215</td>
<td>1.859</td>
<td>.064</td>
</tr>
<tr>
<td>Response to Intrusions Questionnaire (RIQ)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suppression</td>
<td>.525</td>
<td>.164</td>
<td>3.204</td>
<td>.002*</td>
</tr>
<tr>
<td>Rumination</td>
<td>.437</td>
<td>.149</td>
<td>2.937</td>
<td>.004*</td>
</tr>
<tr>
<td>Numbing</td>
<td>1.063</td>
<td>.389</td>
<td>2.734</td>
<td>.007*</td>
</tr>
<tr>
<td>Confounding variables</td>
<td>β</td>
<td>SE</td>
<td>t</td>
<td>Sig.</td>
</tr>
<tr>
<td>(Constant) for confounding model</td>
<td>81.845</td>
<td>5.093</td>
<td>16.070</td>
<td>.000*</td>
</tr>
<tr>
<td>Mindfulness FFMQ</td>
<td>-.603</td>
<td>.086</td>
<td>-7.006</td>
<td>.000*</td>
</tr>
<tr>
<td>Social support MOSSS</td>
<td>-.064</td>
<td>.054</td>
<td>-1.172</td>
<td>.242</td>
</tr>
<tr>
<td>General self-efficacy GSE</td>
<td>-.121</td>
<td>.200</td>
<td>-0.604</td>
<td>.546</td>
</tr>
</tbody>
</table>

*p<0.05  β regression coefficient, SE standard error, t-test statistic, Sig significance  ‡wald statistic

A hierarchical stepwise regression analysed whether cognitive and behavioural variables explained variance in PTSD symptom severity scores over and above the variance predicted by mindfulness. The final model (n=266) included five variables to predict PTSD severity (PCL5 total) and was statistically significant, $R^2=.622$, $F(5,260) =85.396$, $p<0.0005$, adj. $R^2 =.614$. The first step of the model included response to intrusions subscales (suppression, numbing and rumination) and explained 52.2% of the variance in PTSD severity. The addition of negative cognitions of self-subscale of PTCI (model 2) led to a statistically significant increase of 10% $R^2=.621$, $F(1,261) =68.784$, $p<.0005$. The addition of mindfulness
total score (model 3), did not lead to a statistically significant increase in the variance of PTSD symptom severity. In the final model, the variables that remained significant were negative cognitions about the self and all subscales of the RIQ (suppression, rumination and numbing/dissociation). Regression coefficients and standard errors of the hierarchical regression model can be found in Table 6.

Table 6: Cognitive behavioural and mindfulness predictors of PTSD symptom severity included in the hierarchical stepwise regression model

<table>
<thead>
<tr>
<th>Model</th>
<th>Unstandardized Coefficients</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>SE</td>
</tr>
<tr>
<td>1</td>
<td>(Constant)</td>
<td>-13.713</td>
</tr>
<tr>
<td></td>
<td>RIQ_ Suppression</td>
<td>.566</td>
</tr>
<tr>
<td></td>
<td>RIQ_ Rumination</td>
<td>1.203</td>
</tr>
<tr>
<td></td>
<td>RIQ_ Numbing/Dissociation</td>
<td>1.642</td>
</tr>
<tr>
<td>2</td>
<td>(Constant)</td>
<td>-13.460</td>
</tr>
<tr>
<td></td>
<td>RIQ_ Suppression</td>
<td>.532</td>
</tr>
<tr>
<td></td>
<td>RIQ_ Rumination</td>
<td>.503</td>
</tr>
<tr>
<td></td>
<td>RIQ_ Numbing/Dissociation</td>
<td>1.123</td>
</tr>
<tr>
<td></td>
<td>PTCI_ Negative cognitions about the self</td>
<td>5.938</td>
</tr>
<tr>
<td>3</td>
<td>(Constant)</td>
<td>-14.650</td>
</tr>
<tr>
<td></td>
<td>RIQ_ Suppression</td>
<td>.534</td>
</tr>
<tr>
<td></td>
<td>RIQ_ Rumination</td>
<td>.503</td>
</tr>
<tr>
<td></td>
<td>RIQ_ Numbing/Dissociation</td>
<td>1.131</td>
</tr>
<tr>
<td></td>
<td>PTCI_ Negative cognitions about the self</td>
<td>6.020</td>
</tr>
<tr>
<td></td>
<td>FFMQ_ Mindfulness</td>
<td>.012</td>
</tr>
</tbody>
</table>

β regression coefficient, SE standard error, t-test statistic, Sig significance

Discussion

This is the first study to investigate whether theoretically derived variables of Ehlers and Clark (2000) cognitive model of PTSD explain unique variance in PTSD symptoms in the context of HG. Of note, the PCL5 PTSD screening questionnaire suggested that 40.6% of the sample reported symptoms consistent with trauma, across a range of time since HG pregnancy (0-100 months). Corroborating with other HG studies that also used self-report measures to assess PTSD symptoms, prevalence rates range from 10% (Poursharif et al. 2008)
to 18% (Christodoulou-Smith et al. 2011). The overall finding that mental health is negatively affected after discontinuation HG is consistent with the broader research literature on HG (Mitchell-Jones et al. 2017; Meltzer-Brody et al. 2017; Fezio et al. 2009). The differences between findings may be explained by the range of sample sizes, PTSD measures and timings of assessments.

When considered alone, sociodemographic and HG clinical risk factors did not significantly predict variance in PTSD symptoms, protective factors alone predicted 31.2% variance and cognitive behavioural predictors alone predicted 62.3%. Mindfulness did not remain a significant predictor of PTSD severity when analysed in the final hierarchical regression model alongside cognitive behavioural predictors, which together predicted 62.2% of the variance in PTSD symptoms. The findings suggest that targeting negative cognitions about the self and ways of responding to intrusions (numbing, suppression and rumination) in psychological treatment should, in theory, substantially reduce distress from PTSD symptoms post-HG.

Considering cognitive behavioural variables of this study, the strongest predictor of PTCI for PTSD symptoms were negative cognitions about the self. Findings from the qualitative research literature around HG further highlight that negative cognitions such as guilt, responsibility shame further add to distress associated with HG (Dean & Bannigan, 2018). All subscales of the RIQ remained significant predictors in the final hierarchical regression model. Response to intrusions is thought to be a critical posttraumatic variable in the maintenance of PTSD (Ehlers & Clark, 2000) and the suppression subscale of the RIQ and the avoidance symptoms of the PCL5 overlap.

Income level and age had a significant negative correlation with PTSD severity, which is consistent with other research on HG (Roseboom, Ravelli, van der Post, & Painter, 2011; Chou, Kuo & Wang, 2008; Mullin et al. 2012), and general risk factors for PTSD in the perinatal period (Grekin & O’Hara, 2014; Forray, Mayes, Magriples & Epperson, 2009). Postnatal social support and general self-efficacy were shown to be negatively correlated with PTSD
symptoms which is consistent with their roles as protective factors against PTSD (Mystakidou et al. 2015; Koopman et al. 2002; Roseboom et al. 2011). Other studies have highlighted the importance of poor social support and relationship status in predicting perinatal anxiety, depression and PTSD following HG (Hammond & Crozier, 2007; Grekin & O’Hara, 2014).

The results of linear regression analyses show that dispositional mindfulness was a significant predictor of PTSD symptom severity, whereas postnatal social support and general self-efficacy were not. In theory, high dispositional mindfulness such as acting with awareness, describing non-judgementally and observing internal and external contexts may be protective against trauma by supporting potentially traumatic memories to be elaborated, contextualised and integrated into autobiographical memory. However, in the final model of the hierarchical regression, mindfulness did not remain a significant predictor of PTSD when cognitive behavioural variables were included, suggesting the power of negative cognitions about the self and responses to intrusions in maintaining PTSD symptoms.

**Strengths and Limitations**

This is the first study to test the validity of Ehlers and Clark (2000) cognitive model of PTSD for women with a history of HG. The finding that 40.2% of women screen as experiencing elevated levels of PTSD symptoms is substantial. The well-powered sample of 266 women who have experienced HG enabled the study to test for various risk factors and protective factors for PTSD. Given that unhelpful cognitive and behavioural strategies predicted 62.2% variance in PTSD symptom severity, this should be addressed primarily by clinicians in specialist perinatal mental health services to prevent PTSD.

The findings should be interpreted considering the study limitations. Internet recruited samples have questionable representativeness given surveys demand literacy, engagement and organisation and it is often difficult to engage women who are younger, poorer and less educated (Furata, Sandall, Cooper & Bick, 2014). However, online data collection is useful for capturing the experiences of the dispersed HG community. The study
might have appealed to women who had difficulties adjusting to HG and were likely motivated by developing research into HG and mental health. Also, the sole reliance on self-report questionnaires might have led to the overreporting of symptoms and overestimated association with PTSD symptoms due to shared method error variance (Slade, 2006). The cross-sectional, retrospective design means that findings are not generalisable to other time points and self-report of HG may have been biased by subsequent postnatal experience and current PTSD symptoms. The lack of a validated retrospective measure of HG is problematic. The Pregnancy-Unique Quantification of Emesis (PUQE) (Koren, Boskovic, Hard, Maltepe et al. 2002; Lacasse, Rey, Ferreira, Morin et al. 2008) is an objective measure that quantifies HG severity at the time of assessment and could be incorporated in future studies.

**Clinical implications**

The management of HG in primary and secondary care is focussed on medical intervention (Matthews, Haas, O’Mathuna & Dowswell, 2015), despite The World Health Organisation (WHO) recommending interventions that target mental health difficulties associated with physical illness (Hosman & Jané-Llopis, 2005; WHO, 2004; NICE, 2015) and RCOG guidance (2016) recommending assessment and referral for psychological support for women who have experienced HG. Our results showed that only 7% of women accessed clinical psychology support, perhaps due to lack of service availability or lack of referrals from healthcare professionals. This is concerning given that poor mental health is a leading cause of maternal mortality in the UK (Knight, Tuffnell, Kenyon et al., 2015) and women may not have the appropriate support for trauma. If health-visitors and midwives routinely ask about psychological wellbeing, it may discourage suppression and encourage supportive listening and signposting for early intervention (RCOG, 2016). This is crucial given that many perinatal services can only support women up to 1-year post-partum and timely intervention may reduce the duration of treatment and potential long-term burden to women, their offspring and society (NICE, 2015).
Cognitive Behaviour Therapy (CBT) for PTSD is likely to be clinically useful for women who have experienced HG (Sockol, 2015; Nilini, Mehralizade, Mayer & Milanovc, 2018; Mendes, Mello, Ventura et al. 2008). To improve access to psychologically informed intervention, CBT principles could be incorporated into antenatal and postnatal groups, while also providing additional peer support. Social support, including family, friends and healthcare professionals, is necessary as an adjunct to treatment (Soltani & Taylor, 2003; Kramer, Bowen, Stewart & Muhajarine, 2013). Early intervention at primary care level antenatally is prudent and may support resilience during HG and adjustment to motherhood postnatally.

While negative cognitions about the self, suppression, numbing and rumination would be most valuable to identify and target in therapy for PTSD; improving mindfulness may be a helpful adjunct intervention. In line with the findings of this study, improving dispositional mindfulness by remaining present focussed rather than ruminating on the impact of HG and reducing catastrophising about the future or experiential avoidance may reduce suppression, a maintaining factor for PTSD (Hall et al. 2016). Mindfulness-based cognitive behaviour therapy (MBCBT) has been useful for women with moderate nausea and vomiting in pregnancy (Faramarzi, Yazdani & Barat, 2015). Acceptance and Commitment Therapy (ACT; Bonacquisti, Cohen & Schiller, 2017; Taylor, Cavanagh & Strauss, 2016) and Dialectical Behaviour Therapy (DBT; Wilson & Donachie, 2018; Kleiber, Felder, Ashby, Scott et al. 2017) are third wave cognitive behavioural therapies (CBT) that include mindfulness as core skills and are effective at reducing psychological distress in the perinatal period.

Women report being disappointed with communication during their appointments and the dismissive and unsympathetic attitudes of healthcare professionals (O’Hara, 2013). Increasing psychological mindedness of the maternity service, by training health-visitors and midwives on HG and perinatal mental health, may improve attitudes towards women with HG (Soltani et al. 2003; Sykes et al. 2013) and prevent trauma postnatally (Olander, McKenzie
An integrated approach addressing physical and psychological distress associated with HG is essential (Poursharif et al. 2008; Kim, Connolly, Cristancho et al. 2009).

**Conclusion**

This study showed that crucial elements of the Ehlers and Clark’s (2000) cognitive model, negative cognitions about the self and responses to intrusions (suppression, rumination and numbing) significantly explain variance in PTSD symptoms following HG when sociodemographic, HG variables and protective factors were controlled. The cognitive model has utility for formulating and informing the psychological treatment of PTSD following HG.

**Acknowledgements**

The authors would like to acknowledge the helpful advice and support of Pregnancy Sickness Support charity. The team at Pregnancy Sickness Support have also kindly assisted in the promotion of this study and we would like to thank them for their support. The authors would also like to extend special thanks to the women who participated in this study.

**Declaration of interest**

The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper. The research was conducted as part of a Clinical Psychology Doctorate programme.

**Ethics**

Ethical approval was granted for the current study by Cardiff University School of Psychology Research Ethics Committee (EC.18.06.12.5310R).
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Paper Three: Critical Reflections on the Thesis Process

Paper three is not intended for publication.

Paper three will critically reflect on elements of the systematic review (paper one) and empirical study (paper two).

Word Count: 4972 (excluding references)
Introduction

The Clinical Psychology training programme sets a requirement to submit three papers which constitute the doctoral large-scale research project (LSRP): an empirical paper, a literature review and a critical appraisal paper, the last of which is described here. The critical evaluation of both the systematic review and empirical paper will focus on the advantages and disadvantages of the research methodology. The paper will consider the implications for clinical practice and future research based on the findings of both the systematic review and empirical paper. The paper will conclude with the proposed plans for dissemination of the research and the author’s reflections regarding personal and professional development from undertaking the LSRP.

Paper One: Systematic Review

Developing a question for a Systematic Review

The systematic review paper focussed on the psychological impact of pregnancy-related illnesses (PRI) on women’s mental health in the perinatal period. The topic was decided in consultation with LSRP supervisors and the author’s perinatal placement supervisor. Feedback from the perinatal team suggested that PRI are somewhat overlooked given they are temporary, especially when mother and baby and mum were physically well postnatally. There is a growing interest in the effects of PRI, but to date, no systematic review bringing these findings together. The author recognised the interest from clinicians to see whether the psychological impact of experiencing an acute PRI has an acute or chronic effect on mental health. Discussions with women who have experienced PRI informed hypotheses of differences in psychological impact following PRI. These included: lack of control and heightened responsibility for having PRI; complicated relationships with a medical professional (lack empathy or sense of negligence); the threat to the wellbeing of mother and baby from both the PRI and secondary obstetric complications; and previous psychological distress.
Therefore, the author hoped that the systematic review would examine:

1. Whether PRI were independent risk factors for worsening mental health in the antenatal or postnatal period or both?

2. Whether the review identified any risk or protective confounding factors?

3. Whether there are differential impacts on psychological wellbeing depending on the PRI?

Hopefully, the review will inform the development of person-focused psychologically informed healthcare practice and research, to ensure women are supported appropriately throughout the perinatal period.

**Literature Search**

Systematic reviews need to utilise an objective, thorough and reproducible search of a range of sources to identify as many studies as possible (Boland, Cherry & Dickinson, 2017). However, the searches needed to be balanced against the authors time, given the review was being conducted in the context of a doctoral training program with additional pressures of clinical placement workload and academic requirements. PROSPERO, the prospective international register of systematic reviews was searched in November 2018, which did not identify upcoming reviews in this area.

**Databases and search terms**

Four databases were searched (EMBASE, Medline, PsycINFO and CINAHL), due to their comprehensiveness and appropriateness for including journals which relate to psychology and healthcare. Email alerts from each database ensured the author was notified of any additional relevant papers, of which, none were identified. Initial search terms were grouped under three main headings: perinatal period, pregnancy-induced illnesses and psychological impact. Search terms were considered through reviewing the literature, and consultation with
a Cardiff University health librarian (Appendix 3). Authors in the field were contacted to check for any research in press or unpublished findings. A researcher at UCLA replied and shared several published papers that focussed on outcomes for children and potential biological risk factors. These were not included in the systematic review.

**Inclusion and exclusion criteria**

The criteria were modified during the selection process to focus only on the perinatal period, to reduce the number of papers in the review and to assess the temporal relationship between PRI and mental health. Some studies were included if they had first postnatal assessments within the perinatal period (up to 12 months postpartum) and had further followed up (15 months to 24 months postpartum). Two studies did not report when postnatal follow up assessments were made, yet, given the timing of data collection, it was assumed that the data was collected within the perinatal period (Christodoulou-Smith et al. 2011 and Senturk et al. 2017). The exclusion criteria were designed to exclude studies that did not control for other factors than the PRI that would likely influence psychological health postnatally. A review of quantitative research was selected due to its importance for comparing psychological impact across studies.

**Quality assessment**

There is not an agreed approach to assessing the quality of studies included in systematic reviews (Pettigrew & Roberts, 2006). The author chose to utilise an appraisal tool based on personal preference, appropriateness for quantitative methodology, and that demonstrated credibility and rigour to findings (Boland et al. 2017). Many quality assessment frameworks for quantitative research were considered including the Newcastle Ottawa (2010); Down and Blacks feasibility checklist (1998); SIGN methodology checklist 3 for cohort studies (2018); STROBE statement for cohort studies (2007) and Joanna Briggs checklist for cohort studies (2017). The Critical Appraisal Skills Programme (CASP) for prospective cohort studies was used because it is a specific quantitative assessment tool that is well-established
in related literature and is a structured approach with prompts which was helpful for the author and could reduce ambiguity for peer inter-rating. The 12 items on the CASP potentially make it more efficient compared to Down and Blacks and STROBE, providing practical advantages for the author. A rating scale was created for each item on the CASP, to provide a summary score of the quality. Although this is not suggested by the CASP authors who designed the checklist as a discussion tool, it facilitated the reviewer’s ability to compare the material. All studies met the criteria from the first two questions to be reviewed in full. The decision was made to appraise papers after data extraction to ensure an unbiased approach (Boland et al. 2017). A peer independently rated 26% of the studies. Minor disagreements related to research design and data analysis were resolved through discussion. The main issue identified from the quality appraisal was scoring the following question: Are the results generalisable to population level (external validity)? The independent variable of PRI was often clearly objectively diagnosed, and some samples were plentiful, and women were recruited from hospital/clinic settings and followed up at home. However, women of low socio-economic status, high ethnic diversity and less educated were underrepresented across studies. Consequently, all studies achieved partial support for this quality domain.

**Data extraction and synthesis**

Data extraction and synthesis were performed by creating separate tables comparing both the methodological characteristics and data analyses, results and limitations across PRI. A standardised data extraction form such as 'PICOS' (population, intervention, comparison, outcomes and study design) would have provided consistency, reduced bias and improved the validity and reliability of data included in the review. However, a peer independently checked data extracted from four studies for thoroughness, which is an approach accepted as a minimum standard for data extraction (Tacconelli, 2010). In future research, the author would hope to recruit a second researcher to independently perform data extraction to reduce potential errors (Buscemi et al., 2006).
Advantages and disadvantages of the broad methodological approach

Definition

A scoping search of the research literature helped to refine the question and identify the classification of PRI. ‘Pregnancy complications’ is the common term used in the research literature and represents ‘health problems that involve the mother’s health, the baby’s health and both’ (CDC, 2018), including ectopic pregnancies, problems with foetal growth and development, death of foetus or stillbirth. ‘Pregnancy-related illness’ was the author’s preferred term and was defined by guidelines for ‘pregnancy complications’ by the Centre for Disease, Control and Prevention (CDC, 2018), The Office on Women’s Health (OWH, 2019), International Statistics Classification of Diseases and Related Health Problems (ICD-10, 2016) and Tommy’s Charity (2019). Most PRI is associated with secondary risks to mother and baby (Appendix 2).

Quality

The author followed Cochrane recommendations that a systematic review should search two or more databases at a minimum; however, there is a possibility that relevant literature is missed within the four chosen databases. Further database searches were beyond the scope for the current review. Low-quality scores on the CASP were present in studies that did not consider or measure potential confounding variables and/or not having a complete enough or long enough follow-up in the postnatal period. However, studies reviewed concerning HDP compared the type of HDP (HELLP, PPROM, severity and timing of eclampsia) with preterm birth and normotensive controls. Thus, clarifying the direct impact of the PRI and associated factors such as prenatal psychological distress and secondary obstetric complications following from PRI. The range of PRI reviewed, and the high-quality rating of most studies (median 19/23, range 12-21) are strengths of the review.

Timing of Assessments
The comparability of psychological impact across PRI was challenging due to different comparison groups, outcomes (occurrence and severity) and a range of questionnaires and timing of assessments. Of the GDM studies, four assessed postnatal depression only once and early postnatally (1, 6 or 8 weeks postnatally). In clinical practice, the perinatal team would monitor women regularly to differentiate between 'baby blues', fatigue, depression and PTSD; therefore, the results should be interpreted with caution.

The clinical implications and directions for future research will be considered in the final section of paper 3.

**Paper Two: Empirical Paper**

Testing a cognitive model to predict posttraumatic stress disorder in women following experiences of Hyperemesis Gravidarum

**LSRP Context**

Hyperemesis Gravidarum (HG) is a condition at the extreme end of the pregnancy sickness spectrum. NICE recommendations for management of Hyperemesis Gravidarum are based on a Royal College of Obstetricians and Gynaecologists (RCOG) guideline: *The management of nausea and vomiting of pregnancy and hyperemesis gravidarum* (RCOG, 2016); an American College of Obstetricians and Gynaecologists (ACOG) Practice Bulletin: *Nausea and vomiting of pregnancy* (ACOG, 2015); and expert opinion in review articles (Clark et al. 2014; Bustos et al. 2017). Pregnancy Sickness Support (PSS) is a charity that supports women with HG and their families to cope physically, mentally and emotionally. The empirical research was designed in consultation with the founder of PSS, who had shared anecdotally how many women who had experienced HG appeared to be experiencing PTSD symptoms.

**Choice of Research Project**

The author was pleased that a HG research project was offered that valued co-production. A family member of the author had experienced psychological distress associated with the debilitating effect of HG. The author was interested in the psychosocial implications
of HG, mainly what factors triggered and maintained the traumatic stress response, with the hope that the findings will have implications for clinical practice and service development.

**Research Objectives**

The empirical paper aimed to develop an understanding of how Ehlers and Clark's cognitive-behavioural model contributed to women's experiences of PTSD following HG. The author engaged with Pregnancy Sickness Support charity, women who had experienced HG, reviewed the existing literature on HG, and presentations from the first International Colloquium on HG conference in October 2017. The author discussed research objectives with the International Collaboration for Hyperemesis Gravidarum Research working group to check whether this research would fit with the priorities of HG research.

Existing research predominately focussed on the psychosocial impact antenatally, qualitative studies of women's experiences of living with HG and the debate of psychodynamic and biological aetiology of HG. The author decided that research which focussed on postnatal impact and utilised psychological theory would be a valued contribution to the evidence base that would inform clinical psychology practice. No previous studies have investigated cognitive variables concerning the potentially traumatic experience of HG. Therefore, a pilot study to investigate the cognitive model for PTSD (Ehlers & Clark, 2000), including the use of dysfunctional cognitive appraisals and behavioural strategies (thought suppression, rumination, and numbing) may further an understanding of the applicability of the cognitive model in the development and maintenance of PTSD following pregnancy complicated by HG. The author became familiar with a recent publication that had tested this model in relation to childbirth (King, McKenzie-Mcharg & Horsch, 2017) and reviewed research of PTSD in the perinatal period. This informed the authors decision to also measure whether mindfulness (Dhillon, Sparkes & Duarte, 2017), general self-efficacy (Bandura, 1997; Luszczynska, Gutiérrez-Doña, & Schwarzer, 2005; Cieslak, Benight, Schmidt,
Luszczynska, et al. 2009) and social support (Soltani & Taylor, 2003; Kramer, Bowen, Stewart & Muhajarine, 2013) were protective factors against PTSD severity.

Advantages and disadvantages of the broad methodological approach used in the present study

Patient and public involvement

The drive to bring patient and public involvement (PPI) into health care research is a positive development. The NHS sets a legitimate expectation for PPI promotion, with specific guidelines for PPI in maternity care (Savory 2010). Timely and effective PPI can inform service design and healthcare innovations. A strength of this research is PPI from conception to dissemination. Whereas a review of six papers on HG by Dean (2016) showed no PPI, although funding and time limitations might have been barriers to PPI.

PPI benefits research within this context as women with HG are a traditionally disenfranchised group, who find it difficult to access the right care and support. Consultation with PSS helped identify how survivors' journey with HG might have been challenging, and their relationship with health care professionals strained. Designing a study that would engage women without offending or alienating or traumatising women was essential.

To prevent unintentional emotional distress, the survey was emailed to four women who had experienced HG to check how they felt completing it postnatally and to ensure the suitability of questionnaires for the target population, also considering the layout and functionality. The feedback highlighted the frustration "I was asked some similar questions by my GP but was then on a waiting list so never got any psychological help" as well as hope for the clinical implications "I hope this survey can make changes to healthcare professionals’ attitude". The researchers thanked participants for their feedback and explained how it could inform future trainees work.

The results were discussed with PSS and service-users in the author’s perinatal placement, which informed methods of dissemination. The author is excited to develop a
podcast for PSS, in collaboration with women who have experienced HG so that women can discuss the research, clinical implications and service developments.

PPI has been a privilege for the author, who gained insight into the historical and political context of HG. However, making decisions to narrow down the focus of the research in context and scope of the LSRP has been difficult, given the many possible avenues of research. Further challenges have included choosing to use psychometrically sound questionnaires which may have some unhelpful language (e.g. lousy coper) and balancing representing the findings in an accessible and sensitive way for women with HG while also writing for academic journals.

**Supervision**

The supervisors supported the author to take ownership of the LSRP, aiding the author's development as an academic, while also discussing the various directions that the research could take within the boundaries of a pilot study for the LSRP. Any comments made about the research by participants were addressed in supervision and used to inform future research arms.

**Online Recruitment**

Online surveys have been widely used to connect with people with health conditions (Keim-Malpass et al. 2014) and to research women’s experiences of HG (Poursharif et al. 2008, Sykes et al. 2013, Dean & O’Hara 2015, Pregnancy Sickness Support & British Pregnancy Advisory Service 2015). Our research, like other HG studies, evidenced that women were highly motivated to engage in HG research, with over 400 women accessing the survey within the first week of an advertisement on Pregnancy Sickness Support website and social media (Facebook and Instagram). PSS is the only national charity for HG, and monthly visits to their website were in the region of 16,000 in 2015 (Lodge, 2015). Women with HG have reported
that online surveys have the benefits of ease, convenience and flexibility and women are motivated to make a difference (Dean & Goddard, 2016).

Closer inspection of the data revealed most participants dropped out after completing about half of the measures. The study gave the option of leaving and returning to the survey, but it appears that once they left the study, participants did not return. It is possible that the nature of the questionnaires was distressing, and they chose not to respond (e.g. measures on trauma). However, this was not fed-back during piloting or by PSS. The survey was lengthy due to several arms of research so it may have been trying for mothers to commit the time or foresee interruptions due to caring for children.

The research may have benefitted from following up non-respondents to assist future studies in understanding this. The final sample of 266 women who had completed six questionnaires entirely was a well-powered sample size given the rare population. Compared to another study testing the cognitive model for PTSD in a perinatal community (King et al. 2017), the sample size was more substantial.

Due to the potentially distressing nature of the study, ethical issues were considered throughout the research design process to show duty of care (BPS, 2014). Informed consent, confidentiality, right to withdraw and anonymising data was detailed in the information sheet (Appendix 6). Participants were informed that they should reflect on the questionnaire items be upsetting; they were encouraged to seek support from their GP or Pregnancy Sickness Support Charity (Appendix 7).

**Inclusion Criteria**

There is no internationally agreed definition of HG distinct to nausea and vomiting in pregnancy. The Royal College of Obstetricians and Gynaecologists (RCOG, 2016) have suggested criteria for diagnosis that includes admission to hospital, weight loss of more than 5% and clinical signs of dehydration. However, women with severe symptoms who do not fit the criteria, or who meet barriers to accessing treatment, may still experience significant
psychological distress and mental health effects (Dean & Murphy, 2015), so all women who have received second level intervention were included in the study (Painter, Boelig, Kelly & Grooten, 2015). Women were not eligible to participate if they were currently experiencing HG as the author was interested in the impact of this experience postnatally.

The women had a range of time since HG experience, and some had experienced HG more than once. Women were instructed to answer the questionnaires concerning their worst HG pregnancy. A woman reported to the author that her experiences of both HG pregnancies impacted her differently, and she would have liked to describe this. The LSRP methodology didn’t allow for this, but it is being considered for future research arms. In retrospect the author would have liked to have asked, where possible, women to include their scores and dates on the PUQE (Lacasse, Rey, Ferreira, Morin and Bérard, 2008) measure from their healthcare appointments from each HG pregnancy. Hospitalisation for HG was assessed retrospectively; however, recall bias is highly unlikely due to the relatively short interval (Vikanes et al. 2010).

**The rationale for data included or excluded for academic submission**

Questionnaires were used that were psychometrically valid and designed to measure psychological constructs concerning the research hypotheses, and that aided comparability to similar research design (King et al. 2017). Questionnaire studies often yield larger study populations compared with studies utilising clinical interviews, although response bias may have been present. The author was careful to avoid the use of 'diagnosis' in the LSRP, instead use the term 'trauma symptoms' as it would be unethical to diagnose PTSD via an anonymous online survey without any contextual factors or structured clinical interview for DSM-5 diagnoses.

There is an emotional impact of completing online surveys and this warranted special consideration and consultation with PSS and women who had experienced HG. For this reason, potential confounding factors such as a history of psychopathology and trauma, birth
trauma, stillbirth or neonatal mortality were not reviewed. As 37.8% variance was not accounted for in the final regression model, perhaps these potential confounding factors would explain further variance in PTSD severity. The research literature highlights how birth complications and complications postpartum may contribute to postnatal PTSD (Andersen, Melvaer, Videbech, Lamont and Joergensen, 2012; Garthus-Niegel et al. 2013; Kjeldgaard et al. 2018; Tan, Zaidi, Azmi, Omar et al. 2014). However, the interplay of HG and birth trauma was beyond the scope of this LSRP.

The author chose to exclude some data from the final empirical submission. Obstetric data such as gravida, parity, miscarriage and termination were excluded from the final submission. None of these variables were significantly associated with PTSD severity. The reasons for termination were not explored, so the author could not assume this was because of HG as other studies have identified (Dean & Murphy, 2015). Anxiety (GAD7) and Depression (PHQ9) were positively correlated with PCL5 and remained significant predictors in the hierarchical regression model. Given they predicted only a small variance in PTSD severity, they are perhaps side effects of negative cognitions and response to intrusions, which predict most variance in PTSD severity. Comorbidity between perinatal anxiety and depression is high (Grigoriadis, de Camps Meschino et al. 2011; Dikmen-Yildiz, Ayers & Phillips, 2017). In this study, 40.2% of women had moderate-severe anxiety, and 34.3% had moderately severe depression, which is a higher prevalence than other HG research (Tan, Vani, Lim & Omar, 2010). There are many reasons why a HG pregnancy may contribute to vulnerability to increased anxiety and depression; including physiological and hormonal changes, physical discomfort, increased stress, uncertainty and fear regarding the health of self and baby and risk of recurrence in future pregnancies which may impact family planning (Wenzel & Stuart, 2011). These findings complement the findings of a meta-analysis that found statistically significantly higher depression and anxiety scale scores in women with HG compared with controls (Mitchell-Jones, Gallos, Farren, Tobias et al. 2017).
Qualtrics issues

There was no filter to account for women who accessed the survey (656) then didn't start any questionnaires. The sample size for sociodemographic data and cognitive model questionnaires, and all questionnaires that assessed potential protective factors was 321. Qualtrics questions were not forced response, so there was lots of missing data from items of questionnaires, which unfortunately meant the sample size reduced from 321 to 266, but the author is aware that some ethics committees do not permit forced-choice paradigms. Given this sample size was sufficient given the power calculation the author chose to respect the integrity of the data, following advice from supervisors and statistics clinic, rather than a more substantial sample using methodologies for estimating missing data.

Consideration of alternative methodologies that could have been utilised.

A mixed methods approach could be applied to understand posttraumatic growth and effective interventions in the context of HG (Bowling, 2014). An alternative model that could be considered in future research could be the Self-Regulatory Model (SRM) of illness (Leventhal, Phillips & Burns, 2016). This model has been widely used to predict behavioural outcomes, explain psychological consequences, and to help modify illness perceptions and coping strategies (Dempster et al. 2015). The constructs and processes proposed in the SRM have been tested, and illness perceptions have been found to correlate to behaviour and outcomes (Hagger & Orbell, 2003; Hagger, Koch, Chatzisarantis & Orbell, 2017).

Implications for theory

A strength of the empirical study is the use of cognitive behavioural theory and model to assess PTSD, with meta-analytic review demonstrating theoretical robustness (Nilni,
The use of validated measures for the cognitive model PTCI and RIQ, not only helped to understand the research objective but also to contribute to the broader research through replicability and systematic review.

Ehlers and Clark (2000) also hypothesised that memory fragmentation and deficits in peritraumatic processing contribute to PTSD severity. Peritraumatic dissociation has been found to be associated with disorganised narratives of the trauma (Harvey & Bryant, 1999; Murray, Ehlers & Mayou, 2002). This research did not assess this as the measures are best used within 6-12 months of the trauma, and the inclusion criteria of our study did not limit time since HG. However, other studies have shown that nature of trauma memory and dissociation are associated with PTSD (Murray et al., 2002; Halligan, Michael, Clark & Ehlers, 2003; King et al. 2017). Components of dissociation such as reduced awareness of one’s surroundings, derealisation, emotional numbing and disengagement from internal and external contexts may explain encoding deficits contributing to traumatic memories. Mindfulness traits of acting with awareness, describing non-judgementally and observing internal and external contexts may be protective against trauma by preventing dissociation.

**Implications for clinical practice**

The association of pregnancy-related illnesses with psychological distress during the perinatal period, signifies the need for healthcare services to address these difficulties as recommended by current guidelines (NICE, 2015). Both papers highlight the importance of healthcare professionals routinely asking about women’s psychological wellbeing across the perinatal period, providing psychoeducation and supportive listening (Leeners, Rath, Kuse, Neises et al. 2006; RCOG, 2016). Through understanding the psychosocial consequences of PRI, the conversations and interventions provided by healthcare professionals can be optimised. This should inform consultation with families, such that the physical and mental health of the mother is assessed, and early targeted intervention is offered. This may include
referral to Clinical Psychology for interventions such as individual CBT for PTSD (Furata, Horsch, Ng, Bick et al. 2018)-given the empirical study has developed an enhanced understanding of the strength of the predictive value of negative cognitions about the self, suppression, numbing and rumination in maintaining PTSD symptoms. However, despite the guidance and policy drivers advocating for perinatal mental health services, an ongoing challenge for these services is that the provision is patchy and under-resourced (Bauer Parsonage, Knapp, Lemmi et al. 2014). Clinical Psychologists are well positioned to lead on service improvement projects such as integrating care pathways and standardising the mental health training for staff supporting women in the perinatal period. Clinical psychologists can also provide training and consultation to perinatal teams regarding psychological assessment and psychologically informed antenatal and postnatal psychoeducation and skills groups to improve women’s mental health (BPS, 2016).

**Future Research**

In May 2016 an extensive Cochrane review of interventions for HG was published which had no patient and public involvement (PPI) during the entire review process thus rendering the results less meaningful to both the women experiencing the condition and the clinicians treating them (Boelig et al. 2016). Therefore, future research designs might focus on including PPI and mixed methodological studies.

Investigating the interplay of HG, other PRI and birth trauma would be interesting. A prospective study design could control for: prenatal psychological wellbeing, traumatic experiences, birth-related obstetric variables, health status of mother and baby postpartum and measures of parent-baby bonding, to analyse predictors of perinatal mental health. Outcome measures at regular fixed time-points will help to evaluate risk and protective factors for psychological distress better. A review of optimal psychological support in the perinatal period for women who have experienced pregnancy-related illness is required and would guide the expectations of women and their providers.
Dissemination of findings is an essential but often overlooked part of the research process (Kerner, Rimer & Emmons, 2005). The author has considered distribution at a range of levels. At a local level, the systematic review and empirical study will be presented to local perinatal services following their multidisciplinary team meetings. Posters will be co-produced with PSS and the author’s clients who have experienced PRI. These will be displayed in midwifery wards in local health boards and incorporated as part of monthly training for newly qualified midwives. Failure to include participants and the communities associated with the research in the dissemination activity has the potential to undermine the findings and community relationships (Ondenge et al., 2015). Participants in the empirical study were told on their information sheet that the study outcomes would be summarised on the PSS website and associated social media platforms. Professional and academic dissemination activity includes the empirical paper being presented on 14th October 2019 at the International Colloquium on Hyperemesis Gravidarum conference, in Amsterdam. The empirical paper will be submitted to the peer-reviewed British Journal of Clinical Psychology due to the relevant subject matter, the welcoming of studies focused on perinatal mental health and PRI, good impact factor and no publishing fees. The systematic review paper will be submitted to the British Journal of Health Psychology, for the same reasons.

Trainee reflections

The research process, from conception to completion, has developed the author’s competence and confidence as a researcher and clinician. Clinical psychologists are well trained and well placed to support teams and families by contributing to relevant research, although such skills and opportunities are underused in clinical practice (Smith & Thew, 2017).
The author feels more confident in suggesting or leading on research post-qualification, given experiences of ethics applications, SPSS, Qualtrics and PPI with PSS. The opportunity to consult with practitioners, researchers and service-users to design and evaluate the research has been invaluable.

Throughout the process, the author questioned, and continues to ask her epistemological stance. The author's epistemology currently lies somewhere between phenomenology and empiricism, with an openness to varying this approach according to the research or clinical context. The author was drawn to read qualitative studies to have an insight into subjective perspectives and experiences (the phenomenological approach) of women who had pregnancy-related illnesses. The subject matter evoked emotional reactions in the author, who is pregnant, as the author had greater understanding and empathy for the challenging experiences associated with PRI and complications that her clients had experienced. Supervision was constructive to reflect on these issues. The extensive reading to understand the psychosocial and medical impact of pregnancy-related illnesses enabled the author to have a thorough understanding of risk factors for perinatal mental health, which has, in turn, informed the author's clinical practice.

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Appendix 1: Submission Guidelines to British Journal of Health Psychology

The British Journal of Health Psychology publishes original research on all aspects of psychology related to health, health-related behaviour and illness across the lifespan including:

- experimental and clinical research on aetiology
- management of acute and chronic illness
- responses to ill-health
- screening and medical procedures
- psychosocial mediators of health-related behaviours
- influence of emotion on health and health-related behaviours
- psychosocial processes relevant to disease outcomes
- health related behaviour change
- psychological interventions in health and disease
- emotional and behavioural responses to ill health, screening and medical procedures
- psychological aspects of prevention

Authors who are interested in submitting papers that do not fit into these categories are advised to contact the editors who would be very happy to discuss the potential submission.

Papers describing quantitative research (including reviews with quantitative analyses) should be no more than 5000 words (excluding the abstract, reference list, tables and figures). Papers describing qualitative research (including reviews with qualitative analyses) should be no more than 6000 words (including quotes, whether in the text or in tables, but excluding the abstract, tables, figures and references). In exceptional cases the Editor retains discretion to publish papers beyond this length where the clear and concise expression of the scientific content requires greater length (e.g., explanation of a new theory or a substantially new method). Authors must contact the Editor prior to submission in such a case.

All systematic reviews must be pre-registered.

Please refer to the separate guidelines for Registered Reports.

PREPARING THE SUBMISSION

Contributions must be typed in double spacing. All sheets must be numbered.

Cover Letters

Cover letters are not mandatory; however, they may be supplied at the author’s discretion. They should be pasted into the ‘Comments’ box in Editorial Manager.

Parts of the Manuscript

The manuscript should be submitted in separate files: title page; statement of contribution; main text file; figures/tables; supporting information.

Title Page

You may like to use this template for your title page. The title page should contain:
• A short informative title containing the major key words. The title should not contain abbreviations (see Wiley’s best practice SEO tips);
• A short running title of less than 40 characters;
• The full names of the authors;
• The author's institutional affiliations where the work was conducted, with a footnote for the author’s present address if different from where the work was conducted;
• Abstract;
• Keywords;
• Acknowledgments.

Authorship
Please refer to the journal’s Authorship policy in the Editorial Policies and Ethical Considerations section for details on author listing eligibility. When entering the author names into Editorial Manager, the corresponding author will be asked to provide a CRediT contributor role to classify the role that each author played in creating the manuscript. Please see the Project CRediT website for a list of roles.

Abstract
For articles containing original scientific research, a structured abstract of up to 250 words should be included with the headings: Objectives, Design, Methods, Results, Conclusions. Review articles should use these headings: Purpose, Methods, Results, Conclusions. As the abstract is often the most widely visible part of your paper, it is important that it conveys succinctly all the most important features of your study. You can save words by writing short, direct sentences. Helpful hints about writing the conclusions to abstracts can be found here.

Keywords
Please provide appropriate keywords.

Acknowledgments
Contributions from anyone who does not meet the criteria for authorship should be listed, with permission from the contributor, in an Acknowledgments section. Financial and material support should also be mentioned. Thanks to anonymous reviewers are not appropriate.

Statement of Contribution
All authors are required to provide a clear summary of ‘what is already known on this subject?’ and ‘what does this study add?’. Authors should identify existing research knowledge relating to the specific research question and give a summary of the new knowledge added by your study. Under each of these headings, please provide 2-3 (maximum) clear outcome statements (not process statements of what the paper does); the statements for 'what does this study add?' should be presented as bullet points of no more than 100 characters each. The Statement of Contribution should be a separate file.

Main Text File
As papers are double-blind peer reviewed, the main text file should not include any information that might identify the authors.

The main text file should be presented in the following order:

• Title
• Main text
• References
• Tables and figures (each complete with title and footnotes)
• Appendices (if relevant)
Supporting information should be supplied as separate files. Tables and figures can be included at the end of the main document or attached as separate files but they must be mentioned in the text.

- As papers are double-blind peer reviewed, the main text file should not include any information that might identify the authors. Please do not mention the authors’ names or affiliations and always refer to any previous work in the third person.
- The journal uses British spelling; however, authors may submit using either option, as spelling of accepted papers is converted during the production process.

References
References should be prepared according to the *Publication Manual of the American Psychological Association* (6th edition). This means in text citations should follow the author-date method whereby the author’s last name and the year of publication for the source should appear in the text, for example, (Jones, 1998). The complete reference list should appear alphabetically by name at the end of the paper. Please note that for journal articles, issue numbers are not included unless each issue in the volume begins with page 1, and a DOI should be provided for all references where available.

For more information about APA referencing style, please refer to the [APA FAQ](#).

Reference examples follow:

**Journal article**


**Book**

Bradley-Johnson, S. (1994). *Psychoeducational assessment of students who are visually impaired or blind: Infancy through high school* (2nd ed.). Austin, TX: Pro-ed.

**Internet Document**


Tables

Tables should be self-contained and complement, not duplicate, information contained in the text. They should be supplied as editable files, not pasted as images. Legends should be concise but comprehensive – the table, legend, and footnotes must be understandable without reference to the text. All abbreviations must be defined in footnotes. Footnote symbols: †, ‡, §, ¶, should be used (in that order) and *, **, *** should be reserved for P-values. Statistical measures such as SD or SEM should be identified in the headings.

Figures

Although authors are encouraged to send the highest-quality figures possible, for peer-review purposes, a wide variety of formats, sizes, and resolutions are accepted.

[Click here](#) for the basic figure requirements for figures submitted with manuscripts for initial peer review, as well as the more detailed post-acceptance figure requirements.

Legends should be concise but comprehensive – the figure and its legend must be understandable without reference to the text. Include definitions of any symbols used and define/explain all abbreviations and units of measurement.

**Colour figures.** Figures submitted in colour may be reproduced in colour online free of charge. Please note, however, that it is preferable that line figures (e.g. graphs and charts) are supplied in black and white so that they are legible if printed by a reader in black and
white. If an author would prefer to have figures printed in colour in hard copies of the journal, a fee will be charged by the Publisher.

Supporting Information

We strongly encourage submission of protocol papers or trial registration documents, where these are in the public domain, to allow reviewers to assess deviations from these protocols. This will result in reviewers being unblinded to author identity.

Supporting information is information that is not essential to the article, but provides greater depth and background. It is hosted online and appears without editing or typesetting. It may include tables, figures, videos, datasets, etc.

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Note: if data, scripts, or other artefacts used to generate the analyses presented in the paper are available via a publicly available data repository, authors should include a reference to the location of the material within their paper.

General Style Points

For guidelines on editorial style, please consult the APA Publication Manual published by the American Psychological Association. The following points provide general advice on formatting and style.

- **Language**: Authors must avoid the use of sexist or any other discriminatory language.
- **Abbreviations**: In general, terms should not be abbreviated unless they are used repeatedly and the abbreviation is helpful to the reader. Initially, use the word in full, followed by the abbreviation in parentheses. Thereafter use the abbreviation only.
- **Units of measurement**: Measurements should be given in SI or SI-derived units. Visit the Bureau International des Poids et Mesures (BIPM) website for more information about SI units.
- **Effect size**: In normal circumstances, effect size should be incorporated.
- **Numbers**: numbers under 10 are spelt out, except for: measurements with a unit (8mmol/l); age (6 weeks old), or lists with other numbers (11 dogs, 9 cats, 4 gerbils).

Wiley Author Resources

**Manuscript Preparation Tips**: Wiley has a range of resources for authors preparing manuscripts for submission available here. In particular, we encourage authors to consult Wiley’s best practice tips on Writing for Search Engine Optimization.

**Editing, Translation, and Formatting Support**: Wiley Editing Services can greatly improve the chances of a manuscript being accepted. Offering expert help in English language editing, translation, manuscript formatting, and figure preparation, Wiley Editing Services ensures that the manuscript is ready for submission.
## Appendix 2: Description of pregnancy related illnesses

<table>
<thead>
<tr>
<th>Pregnancy Illness</th>
<th>Symptoms</th>
<th>Risk</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperemesis Gravidarum (HG)</td>
<td>Severe persistent nausea and vomiting&lt;br&gt;Weight loss&lt;br&gt;Dehydration&lt;br&gt;Fainting</td>
<td>Malnutrition and anemia</td>
<td>Medication&lt;br&gt;Hospitalization for intravenous fluids and nutrients</td>
</tr>
<tr>
<td>Gestational Diabetes Mellitus (GDM)</td>
<td>Sometimes no symptoms but often extreme thirst, hunger and/or fatigue</td>
<td>Pre-eclampsia&lt;br&gt;Cesarean section&lt;br&gt;Baby born with low blood sugar and jaundice</td>
<td>Meal plans&lt;br&gt;Insulin</td>
</tr>
<tr>
<td>Pelvic girdle pain (PGP)</td>
<td>Pain in the pubic region, lower back, hips, groin, thighs or knees, clicking or grinding in the pelvic area, pain made worse by movement.</td>
<td>None</td>
<td>Physiotherapy</td>
</tr>
<tr>
<td>Infections:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uterine Tract Infection (UTI)</td>
<td>UTI: pain or burning, fever, tiredness or shakiness, nausea, back pain. Sepsis: fever, chills, lower abdominal pain, vaginal discharge</td>
<td>Maternal and fetal morbidity</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>Sepsis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>Tired, pale, faint, short of breath</td>
<td>Low birth weight, premature birth and maternal morbidity</td>
<td>Folic Acid</td>
</tr>
<tr>
<td>Hypertensive disorders of pregnancy (Preeclampsia (PE), HeLLP syndrome (hemolysis elevated liver enzymes and low platelets), PPROM (preterm premature rupture of membranes)),</td>
<td>Swelling of hands and face, stomach pain, sickness, blurred vision, dizziness, headaches.</td>
<td>Risk of placental abruption, preterm birth and infant death</td>
<td>Deliver preterm by planned or emergency caesarean section. If baby is too young, bed rest and medication will be prescribed to manage pressure and prevent seizures.</td>
</tr>
<tr>
<td>Condition</td>
<td>Symptoms</td>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td>----------------------------</td>
<td>--------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Peripartum cardiomyopathy</td>
<td>Fatigue, swollen ankles, shortness of breath, palpitations, swollen neck veins, increased need to urinate.</td>
<td>Heart attack, Heart surgery, Emergency cesarean section</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>Fever, hypotension, uterine tenderness, high heart rate, itchy limbs.</td>
<td>Cerebral palsy of baby, Antibiotics, Emergency cesarean section</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perinatal period</td>
<td>Pregnancy related illness</td>
<td>Psychological impact</td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>--------------------------</td>
<td>----------------------</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TI=(Hyperemesis Gravidarum OR pregnancy sickness OR pregnancy vomiting OR severe nausea and vomiting)</td>
<td>TI=(PTSD OR posttraumatic stress disorder OR posttraumatic stress OR posttraum* OR panic)</td>
<td></td>
</tr>
<tr>
<td>Pregnan* OR post-partum OR post-natal OR peri-natal (words also used without hyphen)</td>
<td>TI=(pre-eclamp* OR preeclamp* OR pregnancy relatedhypertension OR pregnancy-relatedhypertension OR hypertensive disorders of pregnancy)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TI=(gestational diabetes)</td>
<td>TI=(psychological impact OR psychological morbidity OR psychological wellbeing OR mental health)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TI=(HELLP syndrome OR hellp OR haemolysis elevated liver enzymes and low platelets OR hemolysis elevated liver enzymes and low platelets)</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TI=(PPROM OR preterm premature rupture of membranes)</td>
<td>TI=(anxiety OR anxiety disorder OR panic OR GAD OR depression OR mood disorders)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TI=(Maternal sepsis OR toxemia OR infection)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TI=(UTI OR urinary tract infection)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TI=(Peripartum cardiomyopathy)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TI=(Chorioamnionitis OR intra-amniotic infection)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TI=(Pelvic girdle pain OR PGP OR symphysis pubis dysfunction OR SPD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TI= (Anemia OR iron deficiency or folic acid deficiency OR folate deficiency)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Appendix 4 CASP quality review of studies

<table>
<thead>
<tr>
<th>STUDY</th>
<th>AUTHORS</th>
<th>PREGNANCY ILLNESS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kjeldgaard et al. 2017</td>
<td>HG</td>
</tr>
<tr>
<td>2</td>
<td>Christodoulou-Smith et al. 2011</td>
<td>HG</td>
</tr>
<tr>
<td>3</td>
<td>Kjeldgaard et al. 2018</td>
<td>HG</td>
</tr>
<tr>
<td>4</td>
<td>Senturk et al. 2017</td>
<td>HG</td>
</tr>
<tr>
<td>5</td>
<td>Daniells et al. 2003</td>
<td>GDM</td>
</tr>
<tr>
<td>6</td>
<td>Beka et al. 2017</td>
<td>GDM</td>
</tr>
<tr>
<td>7</td>
<td>Zwolinska-Kloc et al. 2017</td>
<td>GDM</td>
</tr>
<tr>
<td>8</td>
<td>Ruohomaki et al. 2018</td>
<td>GDM</td>
</tr>
<tr>
<td>9</td>
<td>Hinkle et al. 2016</td>
<td>GDM</td>
</tr>
<tr>
<td>10</td>
<td>Varela et al. 2017</td>
<td>GDM</td>
</tr>
<tr>
<td>11</td>
<td>Huang et al. 2015</td>
<td>GDM</td>
</tr>
<tr>
<td>12</td>
<td>Kim et al. 2005</td>
<td>GDM/HDP</td>
</tr>
<tr>
<td>13</td>
<td>Mautner et al. 2009</td>
<td>GDM/HDP</td>
</tr>
<tr>
<td>14</td>
<td>Hoedjes et al. 2011</td>
<td>HDP</td>
</tr>
<tr>
<td>15</td>
<td>Englehard et al. 2002</td>
<td>HDP</td>
</tr>
<tr>
<td>16</td>
<td>Stamrood et al. 2011</td>
<td>HDP</td>
</tr>
<tr>
<td>17</td>
<td>Gutke et al. 2007</td>
<td>Pelvic Girdle Pain</td>
</tr>
<tr>
<td>18</td>
<td>Goshtasebi et al. 2013</td>
<td>Anemia</td>
</tr>
<tr>
<td>19</td>
<td>Blom et al. 2010</td>
<td>GDM</td>
</tr>
<tr>
<td>Study</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Did the study address a clearly focussed issue? /2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Is the population clear?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Are the factors studied clear?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Are the outcomes clear?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Is it clear whether the study tried to detect a beneficial or harmful effect?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Was the sample recruited in an acceptable way? /2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Was the cohort representative of a defined population?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Was everybody included who should have been included?</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Was the exposure accurately measured to minimise bias? /2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Did they use objective measurements?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Are they valid measures?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Were all subjects classified into exposure groups using the same procedure?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Was the outcome accurately measured to minimise bias? /2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Did they use objective measurements?</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Are they valid measures?</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Were the measurements methods similar in the different groups?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Confounding Factors/4</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Have the authors identified all confounding factors? (Most very thorough except prenatal psychological distress)</td>
<td>P</td>
<td>p</td>
</tr>
<tr>
<td>Have the authors considered all their confounding factors in the design and/or analysis?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Follow-up/4</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td><strong>Was the follow up of subjects complete enough?</strong></td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td><strong>Were the persons who dropped out or lost to follow up analysed to check whether their leaving would impact overall findings?</strong></td>
<td>Y</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Was the follow up of subjects long enough?</strong></td>
<td>Y</td>
<td>ND</td>
</tr>
<tr>
<td><strong>Results/3</strong></td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td><strong>Were confidence intervals given?</strong></td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td><strong>Are the design and method sufficiently flawed to make results unreliable? (No=1)</strong></td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td><strong>Can the results be due to bias, chance or confounding factors? (No if adjusted for the ones they’ve measured=1)</strong></td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td><strong>Are the results generalisable to population level (external validity)? /2</strong></td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Do the results fit with other available evidence? (if Y &amp; N I have scored Y)/2</strong></td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total Quality Score across 12 quality domains /23</strong></td>
<td>19</td>
<td>16</td>
</tr>
</tbody>
</table>

*ND not defined, NA not applicable, P partly*
Appendix 5 Submission guidance for British Journal of Clinical Psychology

1. SUBMISSION

Authors should kindly note that submission implies that the content has not been published or submitted for publication elsewhere except as a brief abstract in the proceedings of a scientific meeting or symposium.

Once the submission materials have been prepared in accordance with the Author Guidelines, manuscripts should be submitted online at http://www.editorialmanager.com/bjcp

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2. AIMS AND SCOPE

The British Journal of Clinical Psychology publishes original research, both empirical and theoretical, on all aspects of clinical psychology:

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- aetiology, assessment and treatment of the whole range of psychological disorders irrespective of age group and setting
- biological influences on individual behaviour
- studies of psychological interventions and treatment on individuals, dyads, families and groups

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The Journal is catholic with respect to the range of theories and methods used to answer substantive scientific problems. Studies of samples with no current psychological disorder will only be considered if they have a direct bearing on clinical theory or practice.

The following types of paper are invited:

- papers reporting original empirical investigations;
- theoretical papers, provided that these are sufficiently related to empirical data;
• review articles, which need not be exhaustive, but which should give an interpretation of the state of research in a given field and, where appropriate, identify its clinical implications;
• Brief Reports and Comments.

3. MANUSCRIPT CATEGORIES AND REQUIREMENTS

Articles should be no more than 5000 words (excluding the abstract, reference list, tables and figures) and any papers that are over this word limit will be returned to the authors. Appendices are included in the word limit; however online appendices are not included.

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Parts of the Manuscript

The manuscript should be submitted in separate files: title page; main text file; figures/tables; supporting information.

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iii. The full names of the authors;
iv. The author's institutional affiliations where the work was conducted, with a footnote for the author’s present address if different from where the work was conducted;
v. Abstract;
vi. Keywords;
vi. Practitioner Points;
viii. Acknowledgments.

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Abstract
Please provide a structured abstract of up to 250 words under the headings: Objectives, Methods, Results, Conclusions. Articles which report original scientific research should also include a heading 'Design' before 'Methods'. The 'Methods' section for systematic reviews and theoretical papers should include, as a minimum, a description of the methods the author(s) used to access the literature they drew upon. That is, the abstract should summarize the databases that were consulted and the search terms that were used.

Keywords
Please provide appropriate keywords.

Practitioner Points
All articles must include Practitioner Points – these are 2-4 bullet points, following the abstract, with the heading ‘Practitioner Points’. These should briefly and clearly outline the relevance of your research to professional practice. (Please include the 'Practitioner Points' in your main document but do not submit them to Editorial Manager with your abstract.)

Acknowledgments
Contributions from anyone who does not meet the criteria for authorship should be listed, with permission from the contributor, in an Acknowledgments section. Financial and material support should also be mentioned. Thanks to anonymous reviewers are not appropriate.

Main Text File
As papers are double-blind peer reviewed, the main text file should not include any information that might identify the authors.

The main text file should be presented in the following order:

i. Title
ii. Main text
iii. References
iv. Tables and figures (each complete with title and footnotes)
v. Appendices (if relevant)

Supporting information should be supplied as separate files. Tables and figures can be included at the end of the main document or attached as separate files but they must be mentioned in the text.

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- The journal uses British/US spelling; however, authors may submit using either option, as spelling of accepted papers is converted during the production process.

References
References should be prepared according to the Publication Manual of the American Psychological Association (6th edition). This means in text citations should follow the author-date method whereby the author’s last name and the year of publication for the source should appear in the text, for example, (Jones, 1998). The complete reference list should appear alphabetically by name at the end of the paper. Please note that for journal articles, issue numbers are not included unless each issue in the volume begins with page 1, and a DOI should be provided for all references where available.

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**Book**
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Appendix 6: Participant Informed Consent

Informed Consent

Hello, you have been invited to take part in a Cardiff University Clinical Psychology research study focusing on the psychological impact of having experienced Hyperemesis Gravidarum.

Before you decide if you would like to take part it is important that you understand why the research is being done and what it will involve for you.

Reason for conducting this research

This study is being conducted to find out more about the impact of people’s experience of Hyperemesis Gravidarum on their psychological wellbeing. It is hoped that this research will inform healthcare professionals of the psychological impact of HG and provide some clinical recommendations to improve perinatal psychological support for women who experience HG during pregnancy.

Can I take part?

You are invited to participate in this study if you meet the following criteria:

a) You are a woman over the age of 18
b) If you speak English
c) If you have sought medical support (e.g. visiting your GP or referred to hospital) for your severe morning sickness/Hyperemesis Gravidarum.

If you meet the above criteria, please continue reading this page to find out more about this research. If you would like to participate, please tick the informed consent box at the end the page. Once you have ticked the box, the online questionnaire will open for you to complete.
What will happen if I take part?

You will be asked to complete a secure online questionnaire. All responses to the questionnaire are confidential. The questionnaire will take X minutes to complete. We will contact you again in six months time and ask you to complete the questionnaires one final time. This is to explore how psychological wellbeing may change over time. At the end of the study, if you agree, you will be entered into a prize draw to win one of six £50 amazon vouchers. This is to acknowledge the time you have taken out form your day to participate and to show you our appreciation for this.

I understand that the personal data will be processed in accordance with GDPR regulations (see privacy statement below).

If you have a difficulty or disability which means that accessing this study online is troublesome for you, then additional paper or telephone access can be made available. Please contact Hayley or Lisa for more information.

Do I have to take part?

Your participation in this study is entirely voluntary.

We may wish to contact you in the future to collect further information, this is helpful as it can allow us to see if and how things change over time. If you are willing to be contacted in the future, then you will be invited to leave your email address at the end of the survey. If you leave your email address your data will be stored confidentially and if you would like us to delete your data in the future, then we will be able to. If you do not leave your email, your responses will be stored anonymously so we will not be able to identify and withdraw your data once it has been entered into Qualtrics (this survey program).

What are the risks of taking part?

This research has been reviewed and approved by Cardiff University School of Psychology Ethics Committee. The questionnaire has been tested by several members from the charity Pregnancy Sickness Support. It is not expected that this study will cause any distress, but should reflecting on the questionnaire items be upsetting, you are encouraged to seek support from your GP or Pregnancy Sickness Support Charity. A list of support organisations will be provided at the end of the survey. If there is a disclosure of risk during the study process, then researchers will need to break participant confidentiality in line with risk and safeguarding procedures. This is to ensure the safety of participants throughout.
How will information about me be used?

The results of the study will be written up as part of a Clinical Psychology Doctorate project and may be published in professional journals and/or shared at relevant conferences. A general summary of the findings will be shared through Pregnancy Sickness Support charity’s website. You will not be identified by name in the dissemination of the results. If you would like to receive a copy of the final report when it is completed, please follow the link at the end of the survey.

Who will have access to information about me?

Survey responses are confidential as the Qualtrics system automatically generates numerical code for each participant. All research data will be stored in accordance with national policy ad legislation (The Data Protection Act_1998) and BPS Ethics guidelines for internet-mediated research (BPS, 2013). Any email addresses provided by participants for follow up studies in the future will be stored in secure password protected file that is not connected to their questionnaire data. The researcher and research supervisors will have access to the electronic research data. Research data will be stored for 15 years after completion of the study for academic purposes in accordance with Cardiff University Policy and destroyed thereafter.

What is there is a problem, or you have further questions?

If you have any concern or require additional information about any aspect of this study, please contact the researcher or research supervisor. If you would like to complain about this project, please contact Cardiff University School of Psychology Ethics Committee.

Researchers:

Hayley MacGregor, Trainee Clinical Psychologist
Email: MacGregorH@cardiff.ac.uk

Lisa Garvin, Trainee Clinical Psychologist
Email: GarvinL@cardiff.ac.uk

Research Supervisors:

Dr Helen Penny, Senior Research Tutor, Doctorate in Clinical Psychology, Cardiff University
Email: pennyH@cardiff.ac.uk

Dr Cerith Waters, Clinical Psychologist, Lecturer Cardiff University
Email: watersCS@cardiff.ac.uk

Complaints:

Cardiff University School of Psychology Ethics Committee
Ethics Secretary Mark Jones
Email: psychethics@cardiff.ac.uk

Please declare below that you are providing informed consent

[ ] I have read the above participant information and I therefore agree to provide my consent to participate in this study
[ ] I provide my consent to be contacted in the future for potential follow up research
Privacy Notice:

The information provided will be held in compliance with GDPR regulations. Cardiff University is the data controller and Matt Cooper is the data protection officer (inforequest@cardiff.ac.uk). The lawful basis for processing this information is public interest. This information is being collected by Hayley MacGregor and Lisa Garvin.

The information on the consent form will be held securely and separately from the research information. Only the researchers will have access to this form and it will be destroyed after 7 years.

The research information you provide will be used for the purposes of research only and will be stored securely. Only the principal researchers Hayley MacGregor and Lisa Garvin and their research supervisors Dr Helen Penny and Dr Cerith Waters, will have access to this information.
Appendix 7: Participant Debriefing Form

Psychological Impact of experiencing Hyperemesis Gravidarum

Debriefing Information Sheet

Thank you very much for taking part in this study.

We hope you found it interesting.

It is hoped that this research will inform healthcare professionals of the psychological impact of Hyperemesis Gravidarum (HG) and provide some clinical recommendations to improve support for women who experience HG during pregnancy. The findings will be published on Pregnancy Sickness Support website.

Further Support

Reflecting on your experience of having had Hyperemesis Gravidarum and the impact on your wellbeing may have been difficult for you. This is understandable and you may feel low after taking part in this questionnaire. If you do feel upset here are some suggested sources of support, you may want to consider calling upon:

- Your friends and family may be able to provide you with immediate support.
- Your GP is also a potential source of support if you feel upset about what has been discussed for a longer than you feel comfortable with.
- Your GP can refer you to a Clinical Psychologist for support to talk through any difficulties that you experience and support you to cope with these.
• There are also a number of organisations and charities that offer support. You may find some of these helpful.

**Pregnancy Sickness Support (www.pregnancysicknesssupport.org.uk)**

Pregnancy sickness support are a national Support Network for women suffering any degree of nausea and vomiting in pregnancy to access support and comfort at times of isolation and distress. The network is made up of volunteers who know first-hand the trials of nausea and vomiting in pregnancy. The website also provides information on treatments to discuss with your doctor and advice for coping strategies at home. The website hosts an online forum where you can access support from a number of women at almost any time of the day or night. PSS has developed leaflets and information for carers and partners and carers can register with their forum to access an area specifically for them.

PSS Helpline - 02476382020

Lines are open 9am-4.30pm Monday to Friday.

**Mindline (https://www.mind.org.uk/)**

Mindline is a confidential listening service to support anybody who is in distress. Mindline can guide you where to get help, discuss medication and alternative treatments, offer advocacy and look for details of help and support in your own area.

Mindline- phone 0300 123 3393 or text 86463

Lines are open 9am to 6pm, Monday to Friday (except for bank holidays).

**The Samaritans (www.samaritans.org)**

The Samaritans is a national charity and the co-ordinating body for the 201 Samaritans branches across the UK. The Samaritans aims to help alleviate emotional distress- you do not have to be suicidal to call

Samaritans helpline- call 116 123 from any phone for free

Lines are open 24 hours a day, 365 days a year.

If you have any further questions in relation to this study please contact us on the details below.
Contact details:
Name: Hayley MacGregor, Trainee Clinical Psychologist
Email: MacgregorH@cardiff.ac.uk
Address: Doctorate in Clinical Psychology, 11th Floor, Tower Building, School of Psychology, 70 Park Place, Cardiff, CF10 3AT

Name: Lisa Garvin
Email: GarvinL@cariff.ac.uk
Address: Doctorate in Clinical Psychology, 11th Floor, Tower Building, School of Psychology, 70 Park Place, Cardiff, CF10 3AT

If you have any concerns that you would like to raise about the research, you can also contact our academic supervisor:

Contact details:
Name: Dr Helen Penny, Senior Clinical Tutor Cardiff University
Email address: PennyH@cardiff.ac.uk
Address: Doctorate in Clinical Psychology, 11th Floor, Tower Building, School of Psychology, 70 Park Place, Cardiff, CF10 3AT.

Thank you again for taking the time to participate

Privacy Notice: All personal data will be processed in accordance with GDPR regulations

The information provided will be held in compliance with GDPR regulations. Cardiff University is the data controller and Matt Cooper is the data protection officer (inforequest@cardiff.ac.uk). The lawful basis for processing this information is public interest. This information is being collected by Hayley MacGregor and Lisa Garvin. The information on the consent form will be held securely and separately from the research information. Only the researchers will have access to this form, and it will be destroyed after 7 years.

The research information you provide will be used for the purposes of research only and will be stored securely. Only the principal researchers Hayley MacGregor and Lisa Garvin and the research supervisor’s Dr Helen Penny and Dr Cerith Waters, will have access to this information.