The contribution of life events to depression, adjusted for anxiety and somatic symptoms, in mothers during the perinatal period: a prospective cohort study

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The candidate confirms that the work submitted is his/her own and that appropriate credit has been given where reference has been made to the work of others.

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Abstract

There is evidence that life events experienced during the perinatal period, such as relationship breakdown, increase the risk of depression. In addition, clinical comorbidity with anxiety and somatic symptoms is common during the perinatal period and is associated with more negative outcomes for the mother and child. However, few studies have investigated the association between life events and depression symptoms whilst controlling for comorbidity with anxiety and somatic symptoms.

This study aimed to explore the associations between the number and type of life events and depression symptoms across the perinatal period, whilst controlling for age, deprivation levels, comorbid anxiety and somatic symptoms. Cross-sectional associations were explored at three time-points during the perinatal period (26 weeks pregnancy, 8 weeks postnatal and 1 year postnatal) and prospective associations were explored between life events during pregnancy and postnatal depression symptoms.

Data from 917 women who took part in the Born and Bred in Yorkshire population cohort study between 2011-2015 were analysed. Depression, anxiety and somatic symptoms were assessed by the PHQ-8, GAD-7 and PHQ-15 respectively. Life events were assessed using the LTEQ which is a 12-item checklist measure.

Results showed that specific types of life events were stronger predictors of perinatal depression symptoms than the number of life events alone. In particular, life events such as relationship breakdown and serious financial problems in the preceding six months were associated with concurrent perinatal depression symptoms in the cross-sectional analyses. The prospective analyses showed that serious problems in a woman's social network (close friends and relatives) that occurred during pregnancy and soon after childbirth increased the likelihood of experiencing postnatal depression by approximately three times (OR 2.8-3.7). Moreover, problems in a woman's social network during pregnancy were also shown to increase the risk of postnatal depression independently to depression, anxiety and somatic symptoms during pregnancy.

Significant interpersonal and financial life events increase the risk of depression in women during the perinatal period. The results of this study are relevant to public health policymakers and suggestions for clinical implications and further research are discussed.

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List of Abbreviations

BaBY	Born and Bred in Yorkshire
CI	Confidence intervals
DSM-V	Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition)
EPDS	Edinburgh Postnatal Depression Scale
GAD-7	Generalised Anxiety Disorder (7 items)
GP	General Practitioner
IAPT	Improving Access to Psychological Therapies program
ICD-10	International Classification for Diseases
LEDS	Life Events and Difficulties Schedule
LTE-Q	List of Threatening Experiences Questionnaire
M	Mean
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
OCD	Obsessive Compulsive Disorder
OR	Odds ratio
PD	Panic Disorder
PHQ-15	Patient Health Questionnaire – Somatisation Module (15 items)
PHQ-8	Patient Health Questionnaire – Depression Module (8 items)
PRIME-MD PHQ	Primary Care Evaluation of Mental Disorders Patient Health Questionnaire
PTSD	Post-traumatic Stress Disorder
SD	Standard deviation
SF-20	Short Form General Health Survey
VIF	Variance inflation factor

Introduction

This chapter will begin by reviewing the social and policy context of perinatal mental health in England. It will particularly highlight perinatal depression as a major public health concern and describe what is currently known about perinatal depression including its symptomatology, prevalence and clinical comorbidity with other disorders. It will then review the role of life events in contributing to depression during pregnancy (antenatal depression) and in year following childbirth (postnatal depression), as well as other known psychosocial risk factors. Finally, developments in aetiological models of depression are briefly reviewed, before focusing on models of perinatal depression and the potential role of life events.

The social and UK policy context of perinatal mental health

Mental health difficulties during pregnancy and up to the first year after childbirth are referred to as perinatal mental health problems. Perinatal mental health difficulties include depression, anxiety, obsessive compulsive disorder (OCD), postnatal psychosis and post-traumatic stress disorder (PTSD). Estimates of perinatal mental health difficulties vary between 10-20% of child-bearing women (NHS Improving Quality, 2015). Furthermore, recent estimates suggest that half of all cases of perinatal depression go undetected and, even where a need is detected, 40% of women in England still do not have access to specialist perinatal mental health care in their region (NHS England, 2016).

Failure to provide early and effective interventions can have serious consequences for the mother, child and family. The latest findings from the UK and Ireland Confidential Enquiries into Maternal Deaths (2009-14) indicated that suicide is still the leading cause of direct deaths (deaths arising as a direct result of factors relating to pregnancy and the postnatal period) in the year after childbirth (Knight et al., 2017). Extensive research has shown an association between perinatal depression and adverse outcomes for both mother and child including increased maternal alcohol consumption, difficulties in the couple's relationship, premature birth and low birth weight (Field, 2011; Grote et al., 2010; Hollins, 2007). Indeed, maternal mental health difficulties during pregnancy, birth and the first few years of a baby's life can have a significant impact on a child's emotional, cognitive and physical

development (Stein et al., 2014). Children of mothers with perinatal mental health difficulties are at an increased risk of developmental delay, emotional problems, attachment insecurity, symptoms of attention deficit hyperactivity disorder and conduct disorder, and developing depression in adolescence and later life (Balbierz, Bodnar-Deren, Wang, & Howell, 2015; Glover, 2014; Pawlby, Hay, Sharp, Waters, & Pariante, 2011).

The estimated life-time cost to society due to the impact of perinatal depression and perinatal anxiety (without depression) on mothers and their children is £75,728 and £34,811 per woman respectively (Bauer, Knapp & Parsonage, 2016). The public sector (e.g., NHS, social services) bears a fifth of these costs, with over half the cost resulting from adverse outcomes for the child rather than the mother (Bauer et al., 2016).

The impact of perinatal mental health has recently been considered in public policy. The National Maternity Review recommended a significant investment in perinatal mental health care, an area that has been traditionally underfunded (NHS England, 2016a). Consequently, NHS England aims to make specialist perinatal mental health support available to women in all localities by 2020/21 by committing £365 million towards building capacity in specialist perinatal community services and mother and baby units (NHS England, 2016b). These services will focus on improving early detection, diagnosis and access to specialist care in order to prevent mild symptoms of perinatal mental illness from escalating and to minimise the harm experienced by mothers and their families. These aims were set out in the 'Five Year Forward View for Mental Health' (NHS England, 2014) which details the need to close the gap in approximately 85% of local areas where there is no current provision of perinatal mental health services offering National Institute for Health and Care Excellence (NICE) evidenced interventions.

Much research on perinatal mental health has focused on detecting and identifying risk factors for postnatal depression (Bauer et al., 2016). However, we now know that depression, whenever it occurs in the perinatal period, may have serious adverse consequences for the mother, her partner and the child (Marcus, 2009; Stein et al., 2014; Vigod, Wilson, & Howard, 2016). Therefore, it is important to understand the contributing factors to the aetiology of both antenatal and postnatal depression in order to improve its detection and treatment.

Perinatal Depression

Definition.

Antenatal and postnatal depression refers to depression that has its onset during pregnancy and after childbirth, respectively. The definition of antenatal depression according to the Diagnostic and Statistical Manual of Mental Disorders (5th Edition) (DSM-V) is an episode of depression with its onset during pregnancy (APA, 2013). Postnatal depression is an episode of depression with its onset during the first four weeks after childbirth only (APA, 2013). However, in practice, clinicians tend to use a wider diagnostic period, with support from NHS England which states that postnatal depression can occur at any time in the first year after childbirth ("Postnatal depression", 2016).

Symptomatology.

Depression is the fourth leading cause of disease burden world-wide and is set to become the second by 2020, only behind heart disease (WHO, 2001). Depression is characterised by low mood and feelings of hopelessness that can cause significant distress and impairment in functioning (Pawluski, Lonstein, & Fleming, 2017). For most mothers, having a child is a positive experience. Yet, a significant proportion of mothers experience depressive symptoms before and/or after birth (Yim, Tanner Stapleton, Guardino, Hahn-Holbrook, & Dunkel Schetter, 2015). Depressive symptoms after birth may include the milder and transient "baby blues" that usually occur within a few days of childbirth (O'Hara, 1987; O'Hara, Schlechte, Lewis, & Wright, 1991) and require no intervention (Brockington, 2004), or the symptoms of postnatal depression with its onset within several weeks of childbirth and meeting diagnostic criteria for a depressive episode.

There has been considerable debate in the literature as to whether perinatal depression constitutes a unique disorder or whether it is simply depression that occurs during the perinatal period (Jolley & Betrus, 2007). Although perinatal depression shares similarities with depression experienced at any other time (Pawluski, Lonstein, & Fleming, 2017), there is some evidence that perinatal depression includes broader symptomatology than diagnoses of major depression, including greater anxiety, feelings of failure and hyperarousal (Beck & Indman, 2005; Hendrick, Altshuler, Strouse, & Grosser, 2000) and less sadness and

anhedonia (Fox, Sandman, Davis, & Glynn, 2018). In addition, one study has shown that the symptom profile of depression according to the DSM-V criteria differs between antenatal and postnatal depression. Specifically, antenatal depression was associated with more sleep difficulties; whereas postnatal depression was associated with greater fatigue, feelings of worthlessness and low self-esteem, diminished ability to concentrate, and thoughts of death and suicide (Kammerer et al., 2009). However, the rates of psychomotor retardation or agitation were common to both antenatal and postnatal depression.

Under-identification.

There are several pertinent reasons perinatal depression is still under-identified including a lack of training for healthcare professionals in understanding and detecting perinatal depression, or lack of adequate service provision in the first place (Smith, Gopalan, Glance, & Azzam, 2016). It may also be due to the stigma and shame that prevents a woman disclosing depression during a time when she feels she should be happy (Beck & Gable, 2000).

Another difficulty impeding identification is the conflation of the normal physiological complaints arising from pregnancy with the physiological and emotional symptoms associated with depression (Kammerer et al., 2009). Bowen and Muhajarine (2006) suggest that healthcare professionals may misattribute emotional (e.g., feeling overwhelmed or guilty) and somatic (e.g., lack of energy) symptoms of depression to the physiological and lifestyle changes as a result of having a child. Indeed, there is an expected increase in somatic complaints during pregnancy and in the postnatal period as a result of changes in appetite, sleep or energy relating to physiological changes and childcare responsibilities (Williamson, O'Hara, Stuart, Hart, & Watson, 2015). Many of these are similar to the somatic symptoms of depression, which can make it difficult to differentiate between them in the perinatal period (Simpson, Glazer, Michalski, Steiner & Frey, 2014).

However, increased irritability, fatigue, insomnia, and appetite loss have been shown to be valid indicators of postnatal depression in women, when controlling for overall depressed mood (Williamson et al., 2015). The authors suggest that these somatic symptoms can be used to measure postnatal depressive symptoms, although the scores on these symptoms should be adjusted downward to account for their higher baseline rates in the postnatal population (Williamson et al.,

2015). Indeed, it has recently been demonstrated that the elevation of mild depression symptoms on a self-report measure in pregnant women (scores of 5-9 on the Patient Health Questionnaire – 8; Kroenke & Spitzer, 2002) over the general population may be the result of greater endorsement of somatic symptoms in the measure relating to fatigue (McMahon, Arms-Chavez, Harper, & LoBello, 2017).

Prevalence and time course of perinatal depression symptoms.

A 2005 systematic review analysing diagnoses of depression (assessed by clinical assessment or structured clinical interviews, e.g., Structured Clinical Interview for DSM) in high-income countries estimated antenatal depression prevalence at 18.4% and 12.7% for minor and major depression respectively (Gavin et al., 2005). Postnatal depression estimates within three months after childbirth were 19.2% and 7.1% for minor and major depression respectively (Gavin et al., 2005). The most recent meta-analysis has suggested an overall prevalence of major depression across the perinatal period of 11.9% (95% confidence interval 11.4–12.5%) across high and low-middle income countries (Woody, Ferrari, Siskind, Whiteford, & Harris, 2017). In the general population, estimates of depression symptoms (a PHQ-8 score of 10 or greater) has been estimated to be 8.6% in a sample (*N* = 198,678) in the United States (Kroenke et al., 2009). Table 1 shows available prevalence data for depression symptoms in the general and perinatal populations using the symptom measure (PHQ-8) used in the present study.

Table 1. **Prevalence of depression, anxiety and somatising symptoms in general and perinatal populations**

Screening tool	Disorder	General Population (%)	Perinatal Population (%)	Cut-off
PHQ-8	Depression	8.6[a]	6.1[e]	≥10
GAD-7	Anxiety	5.0[b]	-	≥10
PHQ-15	Somatising	10.3[c], 26.0[d]	23.0[f]	≥10

Note: PHQ-8 = Patient Health Questionnaire -8 (Kroenke et al., 2009);
GAD-7 = Generalised Anxiety Disorder-7 (Spitzer, Kroenke, Williams, & Lowe, 2006);
PHQ-15 = Patient Health Questionnaire-15 (Kroenke et al., 2002).

[a]Kroenke et al. (2009)
[b]Lowe et al. (2008)
[c]Kocalevent, Hinz, & Brähler (2013)
[d]Nordin, Palmquist & Nordin (2013)

[e]Ashley, Harper, Arms-Chavez, & LoBello (2016)
[f]Wilkie et al. (2018)

Precise estimates of the prevalence of perinatal depression (proportion of cases in a population at a given time) have not been reliably determined as prevalence rates vary depending on the timing of the assessment, population samples, the screening tool and clinical cut-off scores used or whether a structured clinical interview leading to a diagnosis was undertaken (Halbreich, 2005; McMahon et al., 2017). Most recently, Woody et al. (2017) showed that prevalence rates were significantly higher when generated from screening tools compared with clinical diagnoses. Low-to-middle income countries also had significantly higher estimates of postnatal depression than high income countries (e.g., 18.7% versus 9.5% respectively), although less research has been conducted in low-to-middle income countries. In addition, meta-analyses have estimated the prevalence of antenatal depression to be at least equal to (Woody et al., 2017), if not greater than (Gavin et al., 2005; Underwood, Waldie, D'Souza, Peterson, & Morton, 2016), postnatal depression, even though it typically receives less attention in the public domain.

Few studies have examined the incidence (rate of occurrence of new cases) of perinatal depression. Gavin et al. (2005) suggest a pooled incidence of major depression of 7.5% antenatally, and 6.5% postnatally. The severity and change in depression symptoms is known to vary across the perinatal period (Mora et al., 2009; Sutter-Dallay, Cosnefroy, Glatigny-Dallay, Verdoux, & Rascle, 2012; Vänskä et al., 2011). Indeed, Bayrampour, Tomfohr, and Tough (2016) identified five groups of symptom trajectories (as identified by screening measures) across the perinatal period in their analysis of a large cohort study: minimal symptoms (26.3%), mild symptoms (51.4%), antenatal symptoms only (10%), postnatal symptoms only (10%), and persistent symptoms across the perinatal period (2.4%). Many women experience depression during the perinatal period as a brief, one-off episode and will recover to previous levels of mental health within a few months (Schmied et al., 2013). Some estimates suggest around 60% of women who experience antenatal depression will not go on to experience postnatal depression (Underwood et al., 2016). However, nearly 7% of women experience persistent depression symptoms from pregnancy to the postnatal period (Underwood et al., 2016).

The time course of depression in the perinatal population appears to follow a similar pattern to that in the general population. A large prospective cohort study of 1338 patients attending primary care in the Netherlands were monitored over 39 months (Stegenga et al., 2012). 174 people were found to have depression at baseline (as assessed by a structured clinical interview) and depression symptoms were assessed subsequently using the PHQ-9. Of the 174 participants depressed at baseline, 17% continued to be depressed at 39 months, 40% had intermittent depression symptoms over the 39 months and 43% had recovered from baseline.

In addition, it is estimated that 40-53% of postnatal depression has its onset after childbirth rather than persisting from pregnancy (Underwood et al., 2016; Wisner, Moses-Kolko, & Sit, 2010). Several studies have pointed to a clustering of postnatal depression onset occurring in the first three months post-childbirth (Cox, Murray, & Chapman, 1993; Wisner et al., 2004). Nevertheless, a substantial proportion of postnatal depression has its onset even prior to pregnancy (e.g., 27%; Wisner et al., 2010) and thus represents recurrent lifetime depression.

Perinatal depression and comorbidity.

Depression, anxiety and somatisation are the most frequently co-occuring disorders in the general population, as well as the perinatal population (Hanel et al., 2009; Misri, Abizadeh, Sanders, & Swift, 2015). Despite this, many studies of perinatal depression do not control for comorbidity which makes it difficult to disentangle the unique risk factors and outcomes associated with comorbid perinatal disorders (Pawluski et al., 2017). Few studies have examined risk factors for clinical comorbidity in the perinatal period but one US study (N = 4451) found that a higher number of life events during pregnancy and delivery at less than 27 weeks pregnancy increased the risk of depression and anxiety comorbidity at 3-9 months postnatal (Farr, Dietz, O'Hara, Burley, & Ko, 2014). There is also evidence to suggest that comorbid disorders during the perinatal period lead to worse clinical and social outcomes than primary diagnoses of a single disorder alone (National Research Council, 2009). Therefore, any assessment of perinatal depression should also include assessment of comorbid symptoms of psychological distress in order to deliver effective treatment strategies that target specific symptoms (NICE, 2011). Comorbid anxiety and somatising disorders with perinatal depression are considered below.

Comorbid anxiety disorders.

Definition and symptomatology.

Recently, research has highlighted the frequent comorbidity of postnatal depression with anxiety disorders (Falah-Hassani, Shiri, & Dennis, 2016; Grigoriadis et al., 2011). The literature has so far focused on the experience of the most common anxiety disorders in the perinatal period such as generalised anxiety disorder (GAD), panic disorder (PD) and obsessive-compulsive disorder (OCD). Although the DSM-V does not recognise perinatal onset for anxiety disorders as a separate condition, as it does for perinatal depression, researchers have tended to classify symptoms as potential perinatal GAD if they have been present for at least one month in the perinatal period (Buist, Gotman, & Yonkers, 2011; Wenzel, Haugen, Jackson, & Brendle, 2005). GAD is characterised by excessive worry that is recurring and intrusive and leads to impaired functioning. GAD in the perinatal period has been shown to include themes revolving around fears of the baby's wellbeing, maternal wellbeing or mortality (Misri et al., 2015). The somatic symptoms of GAD such as fatigue, tension and insomnia may also be confounded with somatic symptoms associated with pregnancy and the care of a baby which can make diagnosis more difficult in the perinatal period.

Prevalence and time course of perinatal anxiety symptoms.

Most research has found similar rates of anxiety disorders in the perinatal and general population, although prevalence tends to be higher in pregnancy than after childbirth (Buist et al., 2011). Anxiety disorders are more prevalent than mood disorders in the general population (Kessler et al., 2005) and perinatal population (Giardinelli et al., 2012; Reck et al., 2008; Wenzel et al., 2005; Wynter, Rowe, & Fisher, 2013). Prevalence estimates vary depending on recruitment strategies, measurement scales and methodology used. Studies using participants from hospital outpatients show a higher rate of generalised anxiety disorders than population epidemiological studies (Misri et al., 2015). However, recent pooled estimates suggest a prevalence of anxiety disorders (without depression) between 4.1% to 16.0% antenatally and 2.4% to 18.0% postnatally (Leach, Poyser, Cooklin, & Gallio, 2016). In the general population, prevalence of anxiety as assessed with the GAD-7

at a cut-off score of 10 or greater indicating moderate anxiety has been estimated to be around 5% (Lowe et al., 2008). The incidence of postnatal anxiety has been reported to be between 2.2% and 8.8% (Borri et al., 2008; Giardinelli et al., 2012; Mota, Cox, Enns, Calhoun, & Sareen, 2008; Reck et al., 2008; Uguz, Gezginc, Kayhan, Sari, & Buyukoz, 2010; Wenzel et al., 2005; Wynter et al., 2013). In the general population, there have been insufficient studies on the incidence rates of anxiety to pool data (Somers, Goldner, Waraich & Hsu, 2006). Table 1 shows available prevalence data for anxiety symptoms in the general and perinatal populations using the symptom measure (GAD-7) used in the present study.

Anxiety is highly comorbid with depression in the perinatal period and the shared clinical symptomatology can be difficult to separate (Skouteris, Wertheim, Rallis, Milgrom, & Paxton, 2009). Estimates of clinically diagnosed depression and anxiety comorbidity have ranged between 2.1% and 32% across the perinatal period (Austin et al., 2010; Fairbrother, Janssen, Antony, Tucker, & Young, 2016; Grigoriadis et al., 2011; Matthey, Barnett, Howie, & Kavanagh, 2003; Reck et al., 2008; Tavares et al., 2012; Wenzel et al., 2005). Estimates of diagnoses of depression comorbidity with other anxiety disorders include: panic disorder (4.4%), specific phobia (14.3%) and OCD (18.7%) across the perinatal period (Grigoriadis et al., 2011). The trajectory and severity of anxiety symptoms also varies within the perinatal period. Bayrampour et al. (2016) found five groups of anxiety symptom trajectories (as assessed by anxiety screening measures) in their longitudinal cohort study: minimal symptoms (54.3%), mild symptoms (32.9%), postnatal symptoms only (4.7%), antenatal symptoms only (6.6%) and persistent symptoms through the perinatal period (1.5%).

Recently, studies have examined the stability of anxiety and depression diagnoses and symptoms during the perinatal period, that is, the extent to which the prevalence of individual symptoms stay the same across time (Heron, O'Connor, Evans, Golding, & Glover, 2004; Prenoveau et al., 2013; Skouteris et al., 2009). Prenoveau et al. (2013) found that mothers with comorbid GAD and major depression in the postnatal period (up to two years postnatal) had the greatest stability of diagnosis compared with primary anxiety or depression disorders, meaning that they were least likely to experience remission of comorbid symptoms during the postnatal period.

Importance of assessment.

A clinical overemphasis on depression in the perinatal period can lead to mothers with anxiety going undetected (Matthey, Barnett, Howie, & Kavanagh, 2003). Detection and intervention is crucial as anxiety and depression can interact in a cycle of comorbidity, with each escalating the other (Sutter-Dallay, Giaconne-Marcesche, Glatigny-Dallay, & Verdoux, 2004). Moreover, early detection and treatment of antenatal anxiety may help prevent postnatal depression developing (Pawluski et al., 2017). Comorbid depression and anxiety is associated with greater severity and duration of symptoms in the general population as well as more negative outcomes for mothers and their children than having depression or anxiety alone (Prenoveau et al., 2013; Rowe, Fisher, & Loh, 2008; van Balkom et al., 2008). Perinatal anxiety contributes to negative child outcomes independently to postnatal depression (Stein et al., 2014), for example, through its impact on foetal neurodevelopment (Van den Bergh, Mulder, Mennes, & Glover, 2005). It is also associated with mothers not breastfeeding and spending less quality time with their baby (Schmied et al., 2013).

Comorbid somatic symptom disorders.

Definition and symptomatology.

Somatic and emotional symptoms are both core components of mood and anxiety disorders and form part of the diagnostic criteria for these disorders (Simon, Gater, Kisely, & Piccinelli, 1996). However, the DSM-V also recognises somatic symptom disorders as a separate disorder characterised by the tendency to express psychological distress in the form of somatic complaints and to seek medical attention for them (Al Busaidi, 2010). Somatic complaints are common and account for approximately half of all visits to primary healthcare, with one third of cases being medically unexplainable symptoms (Gureje, Simon, Ustun, & Goldberg, 1997; Kroenke, & Price, 1993). Somatic symptoms or complaints that are commonly assessed for somatic symptom disorder includes back pain, headaches, chest pain, stomach pain, dizziness, and fainting spells (Hiller & Janca, 2003). To meet the DSM-V criteria for a somatic symptom disorder, somatic symptoms must be very distressing or result in significant impairment in functioning, as well as be accompanied by disproportionate thoughts, feelings and behaviours with regard to

those symptoms for at least six months (APA, 2013). The somatic symptoms may be associated with an underlying medical condition that are exacerbated by psychological distress or they may be medically unexplained symptoms.

Prevalence and time course of perinatal somatic symptoms.

The prevalence of perinatal somatic symptom disorders (as indicated by scores on screening measures or by clinical diagnoses) has not yet been reported in the perinatal population. However, in the general primary care population, the prevalence of all forms of clinically diagnosed somatic symptom disorders has been estimated between 10% to 25% (Hilderink, Collard, Rosmalen, & Oude Voshaar, 2013). Somatic symptom disorders are also often comorbid with depression and anxiety disorders in the general population, with estimates ranging from 20% to 67% (Essau, 2007; Grover & Ghosh, 2014; Leiknes, Finset, Moum, & Sandanger, 2007).

In the perinatal population, one UK population study estimated that 23% of women at 8 weeks postnatal (N = 495) experienced somatising symptoms as assessed by the PHQ-15 (a score of 10 or greater) (Wilkie et al., 2018). Two other studies which have used a version of the PHQ-15 (the 13 somatic item scale from the Primary Care Evaluation of Mental Disorders (PRIME-MD) Patient Health Questionnaire) (Spitzer, Kroenke, & Williams, 1999), which was designed to screen for somatic symptom disorders, found that 21.7% (N = 231) of women during pregnancy and 24.8% (N = 154) of women in the postnatal period reported one or more PHQ somatic symptoms in Ethiopia (Senturk et al., 2012) and 47% (N = 87) of a primary care sample in the United States reported having more than six symptoms during pregnancy (Kelly, Russo, & Katon, 2001). However, these studies did not report the prevalence of women with scores on the PHQ above the clinical cut-off which would indicate the presence of somatic symptom disorders. Other studies have reported the prevalence of individual common somatic symptoms in pregnancy such as nausea, vomiting and fatigue (Chou, Lin, Cooney, Walker, & Riggs, 2003), pregnancy-related physical complaints (Kamysheva, Skouteris, Wertheim, Paxton, & Milgrom, 2008), physical and health-related problems after childbirth (Brown & Lumley, 2000), and culturally-specific general somatic complaints (Fisher, Morrow, Ngoc, & Anh, 2004) with their association with perinatal depression symptoms.

Importance of assessment.

Perinatal mental health research has primarily focused on depression and anxiety whilst the impact of co-morbid somatic symptoms is under-researched (Wilkie, Crawley, Button, Thornton, & Ayers, 2018). Depression, anxiety and somatic symptoms are highly co-morbid but there are unique presentations and functional outcomes associated with each (Kroenke, Spitzer, Williams, & Lowe, 2010; Lowe et al., 2008). In the general population, somatic symptoms are associated with increased healthcare utilisation and impaired functioning (Kroenke, Spitzer, & Williams, 2002). Similarly, high levels of somatic symptoms during the perinatal period are associated with poor emotional wellbeing (Wilkie et al., 2018). Senturk et al. (2012) found that somatic symptoms (as measured by a culturally adapted PHQ-15) and mood or anxiety disorders were independently associated with poor maternal functioning across pregnancy and the postnatal period in low-to-middle income countries. The impact of comorbid somatic symptoms in the perinatal population and their association with life events is an under-researched area (Traviss, Meer, West & House, 2013). However, Traviss et al. (2013) found that non-severe life events and number of children were the best predictors of somatic symptoms of distress as measured by the General Health Questionnaire (GHQ-28; Goldberg & Hillier, 1979).

"SAD" triad.

The increased impairment seen in severe forms of comorbid depression, anxiety and somatisation (the "SAD" triad) in primary care has led some to call for a new diagnostic classification of a single overarching disorder which shares depression, anxiety and somatic symptomatology (Barlow, Allen, & Choate, 2016; Hanel et al., 2009; Lowe et al., 2008). One explanation for the symptom overlap is that depression, anxiety and somatisation may emerge from shared psychological or biological vulnerabilities (Lowe et al., 2008).

The overlap between depression and anxiety was originally conceptualised in the tripartite model put forward by Clark and Watson (1991) to account for their common and distinct components. The tripartite model proposed that depression and anxiety share a non-specific component of 'negative affect' (aversive states, e.g., angry, guilty, afraid, sad, worried) but that depressive disorders are uniquely associated with low 'positive affect' (lack of pleasurable engagement with the

environment: e.g., delighted, enthusiastic), and anxiety disorders are uniquely associated with 'physiological arousal' (physiological hyperarousal symptoms: e.g., trembling, dry mouth, shortness of breath). Support for the model has been found in clinical and non-clinical samples of general depression (Anderson & Hope, 2008) and postnatal depression in inpatient (Cunningham, Brown, & Page, 2016) and community samples (Buttner, O'Hara, & Watson, 2012).

This suggests that the structure of perinatal depression, anxiety and comorbid anxiety and depression is similar to emotional symptoms in the general population (Cunningham et al., 2016). In addition, life events have been found to have differential effects on factors in the tripartite model. A longitudinal study showed that negative life events (as measured by the List of Threatening Experiences Questionnaire; LTE-Q) were associated with increasing negative affect and physiological hyperarousal but had less of an impact on decreasing positive affect (Wardenaar, van Veen, Giltay, Zitman, & Penninx, 2014). Limitations of the tripartite model of depression and anxiety have been addressed by several more detailed models (e.g., including specific anxiety disorders other than GAD) (Mineka, Watson, & Clark, 1998) but they still do not describe how somatic symptoms fit with models of anxiety and depression symptomatology (Goldberg, 2010).

To this end, Simms, Prisciandaro, Krueger, & Goldberg, 2012) investigated the structure of depression, anxiety and somatic symptoms as assessed by a structured clinical interview (Composite International Diagnostic Interview; CIDI) in a large international primary care sample (N = 5433) and found evidence for a hierarchical, bifactor model of depression, anxiety and somatic symptoms. Each disorder had symptoms associated with an overarching 'internalising' factor and one of three specific depression, anxiety or somatic factors. A surprising finding of their study is that the majority of variance relating to anxiety was accounted for by the 'internalising' factor, whereas depression and somatic symptoms had additional meaningful residual variance explained by the specific factors, especially at higher severity levels. This is in contrast to previous models (e.g., Clark & Watson, 1991) which found that depression and anxiety disorders have unique variance independent of a shared 'negative affect' factor. However, the 'internalising' factor in Simms et al.'s (2012) model included variance related to distress, anxious arousal and somatic symptoms and, therefore, is broader than the overarching 'negative affect' factor that has been previously conceptualised in Clark and Watson's (1991) tripartite model of

depression and anxiety. In addition, the model suggests that anxiety symptoms are the least severe manifestation of 'internalising' distress, followed by depression symptoms and, lastly, somatic symptoms (relating to psychological distress) representing the most severe form.

Simm et al.'s (2012) model of the structure of depression, anxiety and somatic symptoms requires further validation in general populations and has not yet been investigated in perinatal populations with comorbid depression, anxiety and somatic symptoms. However, it does suggest that depression, anxiety and somatic symptoms (without physical causes) share a common psychological component whilst still retaining individual clinical features that may have different associations with life events.

Life events

Introduction.

Pregnancy and childbirth can be considered stressful life events in themselves which may contribute to the development of depression symptoms in some women (Biaggi, Conroy, Pawlby, & Pariante, 2016). However, much research has investigated the contribution that additional life events during the perinatal period have on the development of perinatal depression. Life events are significant stressful events that occur in a person's life, for example, a divorce (Lancaster et al., 2010). Life events have long been considered in the aetiology of psychological distress and psychiatric disorders (Craig, 1996). International research over several decades has documented the link between recent stressful life events and the onset and course of depression (Brown & Harris, 1978a; Brown & Harris, 1989; Mazure, 1998; Paykel, 2003), with marked life events preceding 80% of episodes of depression in women in the community (Mazure, 1998). Research has also shown that an episode of depression that has been preceded by a stressful life event is of greater symptomatic severity and associated with greater functional impairment than depression without pre-onset life events (Muscatell, Slavich, Monroe, & Gotlib, 2009).

Generally, the link between life stress and mood disorders has been conceptualised within the stress-vulnerability model (or diathesis-stress model; Spielman, Caruso & Glovinsky, 1987). This posits that life events are stressors that

increase demands on a person's resources and may act as a catalyst for psychological distress in the presence of genetic or psychosocial vulnerabilities. Three main types of life stress have been considered in the research in the general population, namely, life events (marked or minor episodic stressors such as loss of employment), difficulties (chronic stressors such as marital strain) and daily hassles (low-threat difficulties as part of daily life, such as housework).

Research in the general population has also established that certain dimensions of life events are associated with mood disorders. Seminal work by Brown and colleagues demonstrated that events associated with loss, entrapment or humiliation are most strongly associated with depression (Brown, Harris & Hepworth, 1995). On the other hand, life events that are threatening (e.g., health-related events), or involve interpersonal conflict, are associated with anxiety (Marteinsdottir, Svensson, Svedberg, Anderberg, & von Knorring, 2007). The depressogenic (depression-causing) effect of events relating to losses was originally explained by a state of stuck mourning in psychodynamic theory (Freud, 1917). Newer perspectives have emerged from animal models of depression which view the potential loss of status and learned helplessness following loss, humiliation or entrapment events as the depressogenic element (Gilbert, 2006). In the general population, the association between bereavement events or relationship breakdown and the development of depression has been confirmed (Kendler, Hettema, Butera, Gardner, & Prescott, 2003). More recent research has highlighted the greater significance of relationship breakdown (Wright, Hill, Pickles, & Sharp, 2015) and chronic financial strain (Yim et al., 2015) in the onset of perinatal depression.

In addition, personally salient events, that is events that carry an important meaning, are hypothesised to be more depressogenic than other types of life events (Brown, Bifulco & Harris, 1987). One of the first lines of evidence for this came from the work of Brown and colleagues who demonstrated that a negative life event that occurred in the same area as an important life commitment (as identified by the individual) was three times more likely to induce depression than other life events (Brown et al., 1987).

The majority of life stress research in perinatal mood disorders has been in the context of major life events which is the focus of the present study. A recent review concluded that both positive and negative life events showed a small-to-medium association with perinatal depression symptoms (Lancaster et al., 2010).

However, research has also highlighted how chronic stressors and daily hassles contribute to postnatal depression (for a review, see Yim et al., 2015). Interestingly, the presence of ongoing chronic stress appears to make a woman more vulnerable to the effects of a major life event during pregnancy (Hammen, Kim, Eberhart, & Brennan, 2009).

Measurement of life events.

Questionnaires.

The literature on life events and perinatal mental health has been restricted by the widespread use of checklist questionnaires, particularly in large cohort studies. Questionnaires are limited in their ability to gather detailed information on the severity and context of events, and often capture a limited range of acute life events without capturing ongoing daily hassles and chronic strains (Paykel, 1983). However, the LTE-Q (Brugha, Bebbington, Tennant, & Hurry, 1985) was specifically designed to include life events that are likely to be experienced as threatening. The types of major life events that are typically captured in questionnaires include events such as bereavement of a parent or child, loss of job and relationship breakdown. The overall aim is usually to obtain a total score of life events or an indication of which type of life event is associated with depression, without the severity of each life event being assessed.

Importantly, questionnaires often do not capture how life events are related temporally to the onset of mood disorders, although this is improved by longitudinal designs and some studies have modified questionnaires to include questions about dates of events (e.g., the LTE-Q; Donoghue, Traviss-Turner, House, Lewis & Gilbody, 2016). Moreover, questionnaires do not easily elicit the participant's perceptions of the relative dependence or independence of an event (the extent to which an event was a result of a person's own behaviour; for example, initiating a separation). Dependent events have been shown to have a greater association with depression onset than independent events (Kendler, Gardner & Prescott, 2006). Prior to the 1980s, the 43-item Social Readjustment Rating Scale (SRRS) (Holmes & Rahe, 1967) was the main questionnaire utilised in life event research. However, since then, a wide range of briefer checklist scales have been used. One review identified the use of several checklist scales, for example: Pilkonis Life Events scale

(PLES), Social Readjustment Rating Scale (SRRS), Coddington's Life Events Scale (CLES), as well as studies using their own custom life events measure (Swendsen & Mazure, 2000).

Despite these limitations, checklist life event measures have made it possible to conduct large-scale population surveys which have increased our understanding of how the number and type of life events contributes to the risk of developing perinatal depression.

Interview schedules.

Empirical demonstration of the association of life events with depression began with the use of questionnaire surveys. However, the 1970s onwards saw the development of several interview schedules such as the Life Events and Difficulties Schedule (LEDS) (Brown & Harris, 1978b), the Peri Life Events Scale (Dohrenwend, Krasnoff, Askenasy, Dohrenwend, 1978), and the Paykel Interview for Recent Life Events (Paykel, 1997).

The introduction of the use of interview schedules offered a much more comprehensive assessment of life stress. In the general life stress research literature, the LEDS (Brown & Harris, 1978b) is the most widely used and regarded as the 'gold standard' for assessing life stress (Donoghue et al., 2016). The LEDS (Brown & Harris, 1978b) elicits a large range of events including acute and chronic life events, and daily hassles that are significant to the person and those close to them. Through narrative accounts of events, it captures in-depth information about the timing, severity and context of events. The strength of the LEDS is in its emphasis on collecting contextual information around an event and the likely meaning for an individual. The LEDS recognises that the severity of an event depends both on the event itself and the meaning and appraisal of it to the individual (National Research Council and Institute of Medicine, 2009). Only events that precede depression onset and are rated as independent (not under the participant's influence) are examined for their role in the aetiology of depression (Spence et al., 2015). However, it is currently underused in perinatal mental health research (one exception being Traviss, Meer, West & House, 2013) because it is resource-intensive in terms of training and the time needed to administer and rate the schedule.

Important considerations in measurement of life events.

Spence et al. (2015) summarises the main issues with the measurement of life events in research investigating their association with depression, which are also pertinent to studies of perinatal depression. The authors suggest that attempts should be made to capture the full range of events that are likely to be stressful, including events that occur to significant others; for example, an illness in a partner. In addition, the meaning of a life event, and how personally salient the event is to the individual, should also play a central role in in considering whether the event plays an aetiological role in depression onset (Brown, Harris & Hepworth, 1995; Brown et al., 1987).

Research has also shown that the timing of life events in relation to depression onset is important. Generally, major life events that occur in the previous six months to depression onset are considered in its aetiology (Ormel, Oldehinkel, & Brilman, 2001), although Kendler, Karkowski, and Prescott (1998) showed that the majority of depression onset occurred in the month following a major event. The effect of life events on depression is both assumed to accumulate as well as decay over time (Hillegers et al., 2004). Indeed, postnatal depression has been found to be more consistently associated with life events occurring after birth than life events occurring during pregnancy (Swendsen & Mazure, 2000). Similarly, life events that occur during pregnancy are likely to have a bigger impact on antenatal depression than those events that occur before pregnancy (Perlen, Woolhouse, Gartland, & Brown, 2013).

Life events and antenatal depression.

The risk factors for antenatal depression have generally received less attention than postnatal depression in the past. However, the growing awareness of the prevalence of antenatal depression and its association with postnatal depression has fuelled recent research. Two recent reviews of risk factors for antenatal depression have identified life stress as significant predictors of antenatal depression (Biaggi et al., 2016; Lancaster et al., 2010). Lancaster et al. (2010) reviewed studies in high-income countries up until 2008 and found medium associations between life stress (major life events and difficulties) in bivariate analyses (correlational analyses), and small-to-medium associations in multivariable analyses (regression analyses taking into account other confounding variables). However, the review found that only a third of studies controlled for confounding variables. In addition, there was large heterogeneity in the studies in terms of design and measures used

(although the majority were depression screening tools) which made it difficult to summarise the strength of association of particular risk factors with antenatal depression (Lancaster et al., 2010).

Biaggi et al. (2016) reviewed eleven studies in community populations between 2003 and 2015 in low-, middle-, and high-income countries that showed a significant effect of life events with antenatal depression. There was approximately an even split amongst studies using cross-sectional and prospective designs, but all studies used depression screening tools such as the EPDS (cut-offs used varied between 10 to 12 on the EPDS). The cross-sectional studies showed that life events in the year prior to pregnancy (Rubertsson, Waldenström, & Wickberg, 2003; Zelkowitz et al., 2004) and during (Fisher et al., 2010; Glazier, Elgar, Goel, & Holzapfel, 2004; Holzmann et al., 2006; Shakeel et al., 2015; Zelkowitz et al., 2004) were significant predictors of antenatal depression. Specifically, Rubertsson et al. (200) found that two or more life events in the year prior to pregnancy was associated with three times greater odds of having antenatal depression symptoms.

Shakeel et al. (2015) found that three or more life events during a period spanning approximately three months prior to pregnancy and during pregnancy itself was predictive of antenatal depression at 28 weeks pregnancy. There was a large variation in methods of assessing life events amongst studies; for example, two studies used life event measures (Social Stress Indicator; Glazier et al., 2004; PERI Life Events Scale; Rubertsson et al., 2003) or modified existing life event measures (Turner, Wheaton and Lloyd Checklist; Holzman et al., 2006), whilst other studies appeared to generate their own list of major life events (Shakeel et al., 2015; Zelkowitz et al., 2004), with one study having a single open-ended question to identify recent adverse life events in their sample (Fisher et al., 2010).

The prospective studies found that life events in the last year (Husain et al., 2012; Zayas, Jankowski, & McKee, 2003) and during pregnancy were associated with antenatal depression (Fisher et al., 2013, Leigh & Milgrom 2008; Verreault et al., 2014). Moreover, a greater number of life events was associated with persistence of depression symptoms throughout pregnancy (Fisher et al., 2013) and into the postnatal period (Husain et al., 2012), and the number of positive life events in the last year experienced was predictive of lower depression symptoms during pregnancy (Zayas et al., 2003). Again, methods of assessing life events in the prospective studies varied between a single, open-ended question (Fisher et al.,

2013), unspecified major life events (Leigh & Milgrom, 2008) and life event measures (Life Stress Event Scale; Verreault et al., 2014; revised Life Events Questionnaire; Zayas et al., 2003; Life Events and Difficulties Schedule; Husain et al., 2012) within both high-income and low-income countries. This heterogeneity makes it difficult to summarise the quantifiable associations between life events and depression across these studies.

Regarding the type of life events that predict antenatal depression, Agostini et al. (2015) found that bereavement, serious interpersonal problems with close friends or family members, unemployment, financial and housing difficulties (as assessed by the List of Threatening Experiences Questionnaire; Brugha et al., 1985) were associated cross-sectionally with antenatal depression in univariable analyses but not in the multivariable model. A second cross-sectional study (N = 1321) found that having one or more of three main life events during pregnancy (abuse, financial difficulties and substance use problems of either a close friend or the mother herself) was associated with higher depressive symptoms mid-pregnancy (Holzman et al., 2006). Depressive symptoms were further elevated for women who reported early negative childhood experiences as well as recent life events (Holzman et al., 2006). Women in relationships are also at an increased risk of depression in pregnancy if their partners experienced stressful life events (Divney et al., 2012). In addition, a longitudinal study within pregnancy found that pregnancy-related life events increased levels of antenatal anxiety only, whereas non-pregnancy related events increased antenatal depression levels only, and to a much larger effect (Meijer et al., 2014).

Life events and postnatal depression.

Substantial evidence has accumulated in the literature that supports an association between life events and postnatal depression but findings are not always consistent. In a review of 21 well-controlled longitudinal studies, only approximately half showed an association between major life events during pregnancy and postnatal depression, or between life events during the early postnatal period and later postnatal depression (Yim et al., 2015). The other studies either found no association or the associations did not persist in multivariable analyses (see Yim et al., 2015). On the other hand, Yim et al.'s (2015) review identified cross-sectional and other less well-controlled longitudinal studies of which the majority

found associations between life events and postnatal depression. The authors suggest that one possible reason for the mixed findings is that a failure to account for important confounding variables (e.g., maternal education, parity, relationship quality) may have led to spurious associations between life events and depression in many studies. In support of this, the authors also point to several large studies and studies using clinical diagnoses of depression that did not find significant associations in the multivariable analyses between antenatal life events (life events occurring during pregnancy and/or before) and postnatal depression (Milgrom et al., 2008; Oppo et al., 2009; Siu, Leung, Ip, Hung, & O'Hara, 2012).

There is evidence that the timing of life event measurement is important when considering its association to depression. In a review of studies using clinical diagnoses of postnatal depression, Swendsen and Mazure (2000) found that some studies only collected life events during pregnancy in order to predict postnatal depression. These showed weaker (or null) associations with postnatal depression (Hopkins, Campbell, & Marcus, 1987; Martin, Brown, Goldberg, & Brockington, 1989; O'Hara, Neunaber, & Zekoski, 1984; O'Hara et al., 1991), compared to studies that measured life events after childbirth (Areias, Kumar, Barros, & Figueiredo, 1996; Marks, Wieck, Checkley, & Kumar, 1992; Martin et al., 1989; O'Hara, 1986; O'Hara et al., 1984; Yelland, Sutherland, & Brown, 2010). These findings may reflect the impact of longer-term difficulties in adjusting to parenting and partner demands with a newborn that are associated with postnatal depression (Swendsen & Mazure, 2000). More recently, Verreault et al. (2014) found that life events in pregnancy were associated with antenatal depression but not with new onset of postnatal depression.

In addition, research has generally focused on the number, rather than the type, of life events that predict postnatal depression (Agostini et al., 2015). Since Yim et al.'s (2015) published review, a longitudinal study found that relationship-specific life events were a significantly stronger predictor of new onset of depression (N = 52) during the perinatal period than non-relationship life events. However, this particular sample showed particularly high levels of psychosocial risk within their intimate relationships, as assessed by the Psychological Abuse Questionnaire (Moffitt et al., 1997) (Wright et al., 2015). Similarly, a large population-based survey in the United States (US) (N = 5395) found a dose-response relationship with the number of stressful life events reported in the 12-month period before birth and

the risk of postnatal depression symptoms at 4 months post-partum, with the strongest associations for partner-related life events (Stone et al., 2015).

Liu and Tronick (2013) also argued that whilst many studies analyse either the association between specific life events and depression (for example, relationship-specific stressors) or the cumulative effect of life events on depression (the number of events), a stronger determinant may be the spread of events across life domains. In their large US population-based survey (N = 3566), they found that specific life events alone did not predict clinical diagnoses of postnatal depression after controlling for sociodemographic factors in multivariable analyses. Moreover, the cumulative impact of life events required a large amount (six or more) to predict postnatal depression. However, they found that life events occurring over multiple domains (relationships, finances or health) conferred a greater risk of postnatal depression than the actual number of life events (Liu & Tronick, 2013). Consistent with the stress-vulnerability model, one explanation for the finding may be that mothers who experience stressors across multiple domains of their life have less chance of "respite" from stress in other areas of their life, which may result in their increased vulnerability to stress. Nevertheless, other studies have found that certain types (or domains) of life events can, indeed, individually predict postnatal depression (Gross, Wells, Radigan-Garcia, & Dietz, 2002; Lacoursiere, Baksh, Bloebaum, & Varner, 2006), though these studies used depression symptoms collected from screening tools rather than clinical diagnoses of depression. Whiffen (1988) points out that changes in self-report severity of depressive symptoms may be more sensitive to the impact of life stress than changes in clinical diagnoses.

Limitations of life events and perinatal depression research.

Research has largely focused on life events that increase the risk of postnatal depression at the expense of investigating life events that predict antenatal depression, which itself is one of the strongest risk factors for postnatal depression. The evidence for a relationship between life events and perinatal depression has also been complicated by differences between studies in design (cross sectional versus longitudinal, prospective versus retrospective), life event measurement, and possible cross-cultural differences. The majority of studies are cross-sectional which limits inferences of directionality that can be drawn. This is important because although life events are assumed to cause depression (stress causation), depression may also

trigger and maintain certain adverse events as a result of an individual's behaviour (stress generation) (Hammen, 2006).

There is also a lack of standardisation in research studies regarding their definition of depression. Studies of postnatal depression have examined postnatal depression at various points in the year following childbirth (Wisner et al., 2010). In addition, a variety of self-report measures have been used to assess depression. Even within studies using the same self-report measure, the clinical cut-offs used to indicate major depression varies. For example, the Edinburgh Postnatal Depression Scale (EPDS) is the most widely used self-report screening tool used in surveys, but one review found that the clinical cut-off scores used in studies to define depression ranged from 10 to 15 (maximum score is 30) (Woody et al., 2017). Studies of perinatal depression have also sometimes combined both major and minor diagnoses of depression (depression of a clinical and sub-clinical severity, respectively) which may have obscured the effects of risk factors, such as life events, on differing severities of depression (Swendsen & Mazure, 2000).

Other psychosocial risk factors for antenatal depression

The most recent review of antenatal depression risk factors concluded that the following factors are associated with greater antenatal depression symptoms: antenatal anxiety, life events, high perceived life stress, a history of depression or anxiety, lack of partner or social support, history of abuse or intimate partner violence, low education, low income, single status, current/past smoking, low self-esteem, history of child abuse, an unplanned pregnancy and past/current pregnancy complications including past pregnancy loss (Biaggi et al., 2016). Inconsistent associations were found between age, employment and substance abuse. In some studies, both younger and older maternal age were found to predict antenatal depressive symptoms, whilst several studies did not find any effect of age (see Biaggi et al., 2016). Interestingly, a synthesis of several longitudinal studies in Australia and New Zealand (total $N > 20{,}000$) found that it was not young age per se that was associated with depression and poorer outcomes, but that young mothers (<20 years old) were more likely to be socially disadvantaged and having been exposed to multiple early adversities including child abuse and domestic violence (Schmied et al., 2013). Overall, the risk factors identified in Biaggi et al.'s (2016) review corroborate those of an earlier review (Lancaster et al., 2010), but they also

identify important obstetric factors (past or current pregnancy complications) that increase the risk of antenatal depression symptoms.

The literature has highlighted that past and current anxiety disorders are predictive of antenatal depression symptoms, and there is also preliminary evidence that anxiety sensitivity (the fear of anxiety-related sensations) may predict antenatal depression symptoms (Verreault et al., 2014) and postnatal depression symptoms (Fairbrother & Woody, 2007) . Anxiety sensitivity has been found to predispose people to depression in the general population (Cox, Enns, Freeman & Walker, 2001; Rector, Szacun-Shimuzu & Leybman, 2007; Taylor, Koch, Woody & McLeann, 1996). Little research has been undertaken to examine somatic symptoms as a predictor of antenatal depression, although somatic symptoms in the general population have been associated with increased risks of mood or anxiety disorders (Kroenke, Jackson, & Chamberlin, 1997). However, studies have demonstrated that a high number of somatic complaints during pregnancy is a valid predictor of antenatal depression (Apter et al., 2013; Kelly et al., 2001; Nylen, Williamson, O'Hara, Watson, & Engeldinger, 2013; Senturk et al., 2012).

Other psychosocial risk factors for postnatal depression

Much research has focused on the risk factors for postnatal depression, rather than antenatal depression, and several reviews of the literature have concluded that the risk factors for postnatal depression with moderate to strong associations (as reported in terms of Cohen's *d* effect sizes) are a history of depression, antenatal depression or anxiety, negative life events, quality of partner relationship, poor social support, parental stress, low self-esteem and neuroticism (Beck, 2001; O'Hara & McCabe, 2013; O'Hara, & Swain, 1996; O'Hara, & Wisner, 2014; Robertson, Grace, Wallington, & Stewart, 2004; Yim et al., 2015). Risk factors with smaller associations include low socioeconomic status, 'single' relationship status, unwanted pregnancy, obstetric complications and infant health and temperament. This led O'Hara and Wisner (2014) to suggest that, as with depression in the general population, there are three main categories of risk factors for postnatal depression: history of mood disorders, life stressors, and poor social support. Not surprisingly, positive social support may act as an important buffer against the effects of life stress and psychological vulnerabilities (Divney et al., 2012; O'Hara & Wisner, 2014) and, conversely, poor marital support can act as a vulnerability factor in the

presence of stressful life events (Paykel, Emms, Fletcher & Rassaby, 1980). Several studies have shown that being married or being in a stable relationship has a stronger protective effect on women of ethnic minority or lower socioeconomic status (Yim et al., 2015).

Consistently, antenatal depression has been shown to be the largest risk factor for postnatal depression (Leigh & Milgrom, 2008; Rubertsson, Wickberg, Gustavsson, & Radestad, 2005). Studies that have controlled for antenatal depression have frequently found the aforementioned predictors of postnatal depression become non-significant (e.g., Clout & Brown, 2015; Kim, Hur, Kim, Oh & Shin, 2008; Leigh & Milgrom, 2008), suggesting that there are many similarities between risk factors contributing to antenatal and postnatal depression (Yim et al., 2015).

Some studies have also elucidated specific risk factors for women with postnatal depression onset (no depression during pregnancy) which include: artificial reproductive techniques (Giardinelli et al., 2012), higher antenatal depressive symptoms, a history of emotional problems, poor social support during pregnancy, perceiving the delivery to be more difficult than expected (Verreault et al., 2014), low socioeconomic status, life events and pre-pregnancy obesity (Silva et al., 2012). On the other hand, Altemus et al. (2012) found that antenatal depression is more strongly associated with a history of previous depressive episodes, more psychosocial stressors (Altemus et al., 2012), an unplanned pregnancy, past obstetric complications and pregnancy loss, than postnatal depression onset (Biaggi et al., 2016).

Anxiety disorders are significant predictors of depression onset in the general population (e.g., Bittner et al., 2004; Hofmeijer-Sevink et al., 2012; Wittchen, Beesdo, Bittner & Goodwin, 2003) and are the second largest risk factor for postnatal depression in the perinatal population (Rubertsson et al., 2005). Anxiety (during pregnancy or in the past) can independently predict postnatal depression, over and above the role of previous depression (during pregnancy or in the past) (Austin, Tully & Parker, 2007; Heron et al., 2004; Horwitz, Briggs-Gowan, Storfer-Isser, & Carter, 2009; Martini et al., 2015; Sutter-Dallay et al., 2012; Verreault et al., 2014) and is sometimes a stronger predictor than previous depression (Matthey, Barnett, Howie, & Kavanagh, 2003).

Moreover, antenatal anxiety has an enduring effect on the risk for subsequent depression, with studies reporting an increased risk up to two years postnatal (Coelho, Murray, Royal-Lawson, & Cooper, 2011) and even up to five years postnatal (van der Waerden, Galera, Saurel-Cubizolles, Sutter-Dallay, & Melchior, 2015). Notably, antenatal anxiety was the only predictor of persistent depression up to 5 years postnatal in a multivariable analysis of a large French cohort study (*N* = 1807) (Van der Waerden et al., 2015). It is important to recognise, however, that some evidence has pointed to a bidirectional relationship between perinatal anxiety and depression, with depression symptoms mid-pregnancy also predicting increased anxiety symptoms in later pregnancy (Skouteris et al., 2009). However, Prenoveau et al. (2013) assessed women (*N* = 296) at five time points in the postnatal period for diagnoses of depression and anxiety (assessed using the SCID) and found that GAD predicted later comorbid GAD and depression, but that depression did not predict later postnatal GAD, suggesting that postnatal GAD is a risk factor for postnatal depression but not conversely.

Aetiological models of depression

Whilst there is clearly a relationship between life events and depression, the majority of people do not develop depression following a stressful life event, suggesting an important role of individual differences (or vulnerabilities) to depression (National Research Council and Institute of Medicine, 2009). Stress-vulnerability models (or diathesis-stress; Spielman et al., 1987*)* have been used in the literature to explain general depression in the population as well as perinatal depression. The stress-vulnerability paradigm incorporates the multiple biological (for a review of biological predictors of postnatal depression, see Yim et al., 2015) and psychosocial risk and protective factors that are known to interact with each other over time in their contribution to the development of depression (Masten, 2001). Interestingly, studies examining interactions between genetic predispositions to mood disorders (e.g., the serotonin transporter polymorphism gene) and life events have tended to find more significant associations when examining life events using interview methods rather than checklist questionnaires (Uher & McGuffin, 2010).

The aetiology of depression is multifaceted and complex, with multiple presumed causal pathways between factors (Colman & Ataullahjan, 2010). In

particular, the issue of causality with regard to life events is far from straightforward, with the potential for life events to provoke depression, which may then increase the risk of someone experiencing further difficulties and worsening depression symptoms (Tennant, Bebbington, & Hurry, 1981).

Developmental, or life course, models have attempted to take into account the effects of early life adversity, chronic life stress and acute stressful life events on the development of depression. Developmental models of depression have highlighted the role of childhood adversity in representing a general vulnerability to developing mood and anxiety disorders throughout life (Colman & Ataullahjan, 2010; Kendler, Gardner, & Prescott, 2002). In their large US survey, McLaughlin et al. (2010) found that three or more childhood adversities increased the risk of depression among individuals who experienced life events in the last year (N = 34,653). Although the causal mechanisms have yet to be identified, it is hypothesised that childhood adversity leads to chronic dysregulation in the stress response system which increases reactivity to stress (Heim & Nemeroff, 2001) and a potential reduction in emotional regulation or social skills (Kessler, Davis, & Kendler, 1997). Developmental models also assume that there may be a cumulative impact of stressors beginning early on in development that lead to increased vulnerability to depression (Colman & Ataullahjan, 2010). There is also evidence to suggest that childhood adversity is associated with women experiencing a greater number of lifetime traumatic events, life events and reported difficulties in the last year at the time of assessment, particularly marital problems (Kendler et al., 2002).

Models of general depression.

Kendler, Gardner and Prescott (2002) proposed a developmental model of general depression in women based on their analysis of longitudinal risk factors in 1942 female twin pairs. They considered eighteen risk factors known to influence depression covering the developmental lifespan including genetic influences, childhood adversity and environment, personality traits and cognitive biases, history of anxiety and depression, traumatic events, low social support, substance misuse, marital difficulties, recent life events and chronic stress. They found that the three strongest risk factors for the onset of depression in the last year were recent stressful life events (dependent and independent) and neuroticism.

Kendler et al.'s (2002) model has several strengths. First, they report correlation coefficients based on their empirical analysis for each risk factor which means that strengths of associations between risk factors can be judged. For example, recent life events was a stronger predictor of depression in the last year than chronic stress in the last year. Secondly, the model breaks down life events into several detailed categories and models associations between them. For example, specific childhood adversities (e.g., 'childhood sexual abuse',' childhood parental losses) are assumed to increase the likelihood of later life events such as 'lifetime traumatic experiences', and 'dependent' or 'independent life events in the last year'. The model also highlights the role that interpersonal difficulties (history of divorce, marital difficulties) play in the development of depression by leading to more dependent stressful life events in the last year that may trigger depression onset. This is in keeping with the literature on personally salient and loss events being more depressogenic than other events (Brown et al., 1987).

Thirdly, the reciprocal associations between life events and a history of depression (early adversity leading to past episodes of depression which leads to further negative life events) are modelled. Fourthly, the model also links depression and anxiety by including a developmental pathway from early-onset anxiety to later depression based on the evidence of anxiety as a predisposing factor for depression (Breslau, Schultz & Peterson, 1995) and its tendency to be more chronic in nature (stability of symptoms over time) than depression (Stein & Heimberg, 2004).

Nevertheless, Kendler et al. (2002) advise interpreting the model with caution, given that they have modelled risk factors as having a linear and additive impact on depression even though this is unlikely to be the case. Interactions between risk factors were not included in their model due to the greater complexity in interpreting the vast number of possible interactions this would incur.

Models of perinatal depression.

Halbreich (2005) proposed a biopsychosocialcultural model specific to postnatal mood disorders such as depression and anxiety. It updates previous models in its concept of a dynamically evolving vulnerability that is shaped by both positive and negative life experiences, as well as the role of culture in the aetiology and reporting of perinatal mood disorders. Cultural factors have been shown to play an important role in the vulnerability and presentation of perinatal mood disorders (e.g.,

Wittkowsi, Gardner, Bunton, & Edge, 2014). The model also includes pregnancy-specific factors such as the abrupt psychosocial change of motherhood and its associated demands and the sudden change in hormones at birth that are hypothesised to have an impact on some women (Yim et al., 2015). The model also attempts to show how vulnerability is being continuously shaped by life events over time. For example, women who reported negative life circumstances largely limited to their childhood had less severe depressive symptoms in pregnancy than women with multiple exposures to negative life circumstances across their life (Holzman et al., 2006). Nevertheless, women who have experienced childhood abuse are still at an increased risk of perinatal depression than women who have not (Plant, Barker, Waters, Pawlby, & Pariante, 2013).

The model also highlights that positive life events decrease vulnerability by neutralising previous threatening events or increasing positive potential. Indeed, positive life events increase recovery from depression in the general population (e.g., Harris, Brown, & Robinson, 1999). Similarly to Kendler et al.'s (2002) developmental model of depression in women, Halbreich's (2005) model emphasises the role of early life experiences, history of mood disorders and social support, coping mechanisms and life events in altering vulnerability. However, much greater specificity on the nature and strength of relationships in the model based on empirical evidence is needed: for example, exactly how and what "adverse socioeconomic events" specified in the model contribute to vulnerability to postnatal mood disorders. In contrast to Kendler et al.'s (2002) model, Halbreich's model is explicit about the fact that life events may act cumulatively (i.e. past events sensitise the individual further to the effects of future events) rather than additively (where vulnerability increases linearly with life events) on vulnerability to depression, although this is not specified in detail.

Leigh and Milgrom (2008) expand on a psychosocial model of antenatal and postnatal depression that accounts for their finding that antenatal depression can mediate between several risk factors such as history of abuse, negative cognitive bias, antenatal anxiety, low self-esteem and social support, and postnatal depression. They also suggest that these risk factors may lead to the maintenance of antenatal depression and subsequent postnatal depression. Their model also includes direct pathways between antenatal stressors, personal resources, predisposing factors and postnatal depression that do not exhibit their effects through antenatal depression,

though the circumstances in which these factors would not be mediated by antenatal depression were not explored. As such, detail regarding the particular risk factors that are associated with onset of depression in the postnatal period was not addressed.

The developmental models discussed above attempt to model a dynamic interplay between genetic vulnerabilities, psychological and sociocultural factors, including pregnancy-specific factors, but they are limited in detailing the impact of the nature and frequency of life events on antenatal and postnatal depression. They also lack detail regarding the difference in risk factors, including life events, for antenatal and postnatal depression. In addition, although the models acknowledged that interactions are likely to exist between risk factors, for example, the 'buffering' effects of social support on life stress and depression, the direct and moderating effects of different risk factors on perinatal depression have not been conceptualised in any detail.

Psychological processes contributing to vulnerability to depression following life events

Rumination and worry.

Repetitive thought, of which rumination and worry are two manifestations, is a common result of adverse life events and is hypothesised to maintain or exacerbate negative mood (Segerstrom, Tsao, Alden & Craske, 2000). Rumination and worry are highly correlated with neuroticism which is a predisposition to experiencing adverse experiences more negatively (Watson & Clark, 1984). However, rumination and worry are theorised to contribute to depression independently of neuroticism (or negative affect) through its effects on increasing cognitive focus on difficulties (Carver & Scheier, 1990). It has been suggested that rumination is triggered by discrepancies between current events and a person's goals or beliefs about themselves and thus rumination is an attempt at making sense of the discrepancy (Clark, 1996). Although this may initially be functional if it promotes problem-solving, over time, the enhanced cognitive focus on unsolvable problems can lead to depression. Events that challenge emotional security or self-identity have been linked with depression (Segerstrom et al., 2000).

Coping styles.

Lazarus and Folkman (1984) distinguished between problem-focused coping

(e.g., attempting to minimise distress through modifying the stressor or environment) and emotion-focused coping (attempting to minimise distress through cognitive strategies such as distraction). Both forms of coping are adaptive in different situations. A second dimension of coping has been described in the literature as the approach-avoidance dimension to coping (Roth & Cohen, 1986). There is evidence that approach coping (i.e. orienting cognitive and emotional coping strategies towards actively dealing with the stressor) results in lower levels of depressed mood than avoidance coping (cognitive strategies aimed at distancing or detaching the individual from the stressor) (Blalock & Joiner, 2000). An individual's propensity to developing depression following adverse events is mediated through coping styles, personality traits and attributional style (Brewin, 1985). Bebbington (1996) reviewed the evidence for different cognitive attributions (expectations) and their relationship with depression after an adverse experience. Attributions of events that are internal (perceiving the cause to be due to personal factors), stable (perceiving the cause to be persist in an individual's life for a long time) and global (perceiving the cause to be potentially present in all situations) (Abramson, Seligman & Teasdale, 1978).

Transition to motherhood.

As previously discussed, events that challenge a person's self-identity or emotional security can trigger rumination and worry which can lead to depression. The transition to motherhood is a time of significant change in a woman's life and begins during pregnancy where the woman begins to seek information and care for herself and the baby (Mercer, 2004). A woman's maternal identity continues to expand as she overcomes new challenges in motherhood by making connections to more parts of herself and others (Mercer, 2004). Barclay, Everitt, Rogan, Schmied & Wyllie (1997) examined women's experiences of becoming a mother in a grounded-theory study and found that this transition is not only a period of growth but also of change. Nelson (2003) synthesised data from nine qualitative studies exploring the transition to motherhood and identified five core areas of disruption to a woman's life as a result of becoming a mother: relationships, commitments, daily life, self and work. The transition to motherhood involves a complex process where women may experience a period of self-loss, re-evaluation of self and identity transformation (Laney, Lewis Hall, Anderson & Willingham, 2015). Identity is developed in the

context of relationships (e.g., Chodorow, 1978) but there is also the suggestion that women, in particular, look to their web of relationships in helping to define who they are (Gilligan, 1983). Becoming a mother forces women to re-evaluate themselves in relationship to other people and how their changed autonomy, physical condition, relationship with their partner and daily life influences their identity (Laney, Carruthers, Hall & Anderson, 2014). It is not surprising that when a woman's expectations of motherhood or herself as a mother are confronted by a different reality, that internal conflict can arise leading to depression (Choi, Henshaw, Baker & Tree, 2005). In addition, maternal attitudes play an important role in maternal identity. A woman's satisfaction in her mother role has found to be influenced by her maternal competence and her perception of her bond with her infant (Mercer, 2004). Maladaptive or rigid attitudes towards mother have been found to be associated with increased risk of depression and anxiety during the perinatal period (Sockol, Epperson & Barber, 2015).

Summary

In summary, early identification and treatment of perinatal depression is important to safeguarding the wellbeing of the mother, child and family in both the short- and long-term. O'Hara et al.'s (2014) description of the three most important risk factors for postnatal depression, namely a history of mood disorders, life events and poor social support appears to hold for antenatal depression as well. However, longitudinal research following groups of women throughout the perinatal period has started to identify different risk factors for antenatal and postnatal depression. Moreover, research has started to differentiate between antenatal onset, persistent perinatal depression and postnatal onset. Further research is needed as to whether different risk factors are important across these categories (Underwood et al., 2016). There is also an increased recognition of the importance of identifying frequent comorbid clinical disorders with perinatal depression. A number of methodological issues have been highlighted in the literature including differences in life event and depression measurement across studies which may obscure the effects of life events on perinatal depression (Swendsen & Mazure, 2000). Further research is needed using prospective cohort designs, in-depth life event interview schedules (as opposed to questionnaires), and examining interactions between life events and

vulnerability factors to empirically test a stress-vulnerability perspective on perinatal depression (Yim et al., 2015).

The existing stress-vulnerability models of life events and its interaction with biological and psychosocial factors have attempted to address the multifactorial aetiology of perinatal depression. However, they have been unable to fully conceptualise the dynamic relationship between life events and vulnerability to depression in the perinatal period. The present study aimed to further the understanding of the relationships between the number and type of life events and depression across the perinatal period. To the author's knowledge, this was the first study to examine the cross-sectional and prospective associations between life events and perinatal depression symptoms in a population cohort whilst controlling for comorbid anxiety and somatic symptoms.

Research aims

The primary focus of this study was to examine the association between the number and the type of life events experienced and self-reported depression symptoms in the perinatal period in a large population cohort. The unique contribution of life events to perinatal depression symptoms was explored whilst controlling for the effects of age and deprivation levels and comorbid anxiety and somatic symptoms. This was achieved in cross-sectional and prospective analyses. First, the association between recent life events (in the last 6 months) and concurrent depression symptoms was explored cross-sectionally at each of three time-points in the perinatal period (26 weeks pregnancy, 8 weeks postnatally, 1 year postnatally). Secondly, life events occurring during pregnancy to the early postnatal period were examined as predictors of postnatal depression in prospective analyses. Although the inference of causality typically requires experimentation, the prospective analyses enabled an examination of how life events occurring during pregnancy may contribute to later depressive symptoms in the postnatal period while accounting for antenatal levels of depression, anxiety and somatic symptoms.

The aims of the study were as follows:

1. To establish the levels of self-reported depression, anxiety and somatic symptoms in a large population cohort of mothers during pregnancy and in the first year after childbirth.

2. To examine the association between the number and type of life events experienced and perinatal depression whilst controlling for demographic variables and comorbid anxiety and somatic symptoms in a series of cross-sectional and prospective models.

   The second aim was achieved through the following specific objectives to investigate:

   i. Cross-sectional associations between life events and the prevalence of perinatal depression at the three time-points during the perinatal period.
   ii. Prospective associations between life events occurring during pregnancy through to the early postnatal period, and postnatal depression.

Method

Design

This study conducted a secondary analysis on mental wellbeing and life events data collected from women who participated in the BaBY (Born and Bred in Yorkshire) study. This enabled the association between the number and type of life events as risk factors of perinatal depression to be explored both cross-sectionally and prospectively whilst controlling for age, deprivation and comorbid anxiety and somatic symptoms. Associations between risk factors were explored cross-sectionally during pregnancy (approximately 26 weeks), and twice in the year after birth (approximately 8 weeks postnatal and 1 year postnatal).

The BaBY study.

Context.

This study utilised data collected from the BaBY cohort. BaBY is a population-based cohort study designed to gather information about the health and wellbeing of babies born in Yorkshire and North Lincolnshire, as well as their parents. The project spanned 2011 to 2015 and was led by researchers at the University of York (the Mental Health & Addiction Research Group and the Epidemiology & Cancer Statistics Group) and Hull York Medical School in collaboration with local NHS Trusts. Further information about the BaBY study can be found on their website (https://www.bornbredyorks.org/). The project sought to gather a range of clinical outcomes for the parents and the baby throughout the perinatal period from the following sources:

- Maternity notes: information about the pregnancy, birth and the baby's first few days.
- Medical records: information about parents' and baby's health.
- Mental wellbeing questionnaires: completed by mothers and their partners at around 26 weeks pregnancy, 8 weeks postnatal and 1 year postnatal.

The mental wellbeing questionnaires included assessment of depression (Patient Health Questionnaire; PHQ-8), anxiety (Generalised Anxiety Disorder;

GAD-7), somatic symptoms (Patient Health Questionnaire; PHQ-15) and life events (List of Threatening Experiences Questionnaire; LTE-Q).

BaBY participants and recruitment procedures.

The study aimed to invite all women who were booked for delivery, or had their babies born, in any of the four hospitals taking part during the study period: York Hospital; Hull Royal Infirmary; Harrogate District Hospital; and Scunthorpe General Hospital & Goole Midwifery Led Unit. Women were invited to take part in the study, regardless of age or parity, unless there was any reason that they were considered unable to give informed consent. The BaBY study had a target population of around 13,500 births a year across the sites, with an estimated recruitment uptake of greater than 60% of women consenting to the study who were approached (Littlewood et al., 2016). Women were given an information pack containing study information and maternal and partner consent forms at their first antenatal appointment (approximately 12-14 weeks of pregnancy). Partners were welcome to take part in the study if the mother invited them to do so. The parents could choose to consent to all parts of the study or to specific parts only. Copies of the consent forms were sent to the participants' General Practitioners (GP) and kept in the mother's maternity records. There was also the option for women to consent online if they preferred, using a secure website specifically designed for the study. Parents were able to join the study at any stage during pregnancy or in the year following their baby's birth by; for example, responding to advertised information about the study in GP surgeries and antenatal classes run by community midwives. Health visitors could also offer parents study information and consent forms at the routine primary birth visit (approximately two weeks after birth).

Data collection in the BaBY study.

Minimal demographic and biographical data were collected for the women from the study consent forms. After consent to the study was obtained (at approximately 12-14 weeks of pregnancy), a pack of mental wellbeing and life event questionnaires were sent to the women at approximately 26 weeks pregnancy, 8 weeks postnatal and 1 year postnatal along with their own unique identifier code. The questionnaires could either be returned via the self-addressed envelopes

provided or there was an option to complete the questionnaires online using the web link provided and their unique identifier.

Measures

Women were asked to complete four validated self-report questionnaires that assess different aspects of mental wellbeing and their experience of life events at each of the three time-points in the study: 26 weeks pregnancy, 8 weeks postnatal and 1 year postnatal. The use of brief self-report measures is common in large scale studies in order to reduce the completion burden on participants and collect a large amount of data at relatively low cost. However, disadvantages include the greater potential for systematic response biases such as socially desirable responding and acquiescence (the tendency to respond affirmatively e.g., "yes") which may mask the true relationship between variables (Razavi, 2001). It is important to evaluate the psychometric properties of scales with regards to their validity and reliability, and to also consider the implications of potential biases in their construction in any interpretation of results drawn from them (Razavi, 2001). Copies of the measures discussed in the following section can be found in the Appendices.

Patient Health Questionnaire (PHQ-8).

The PHQ-8 is an abbreviated version of the Patient Health Questionnaire-9 (PHQ-9) which is an established and valid diagnostic measure of depressive symptoms that is widely used in primary care, including the United Kingdom's Improving Access to Psychological Therapies (IAPT) program (Kroenke et al., 2009. The PHQ-9 was developed as a brief self-report screening tool for major depression out of the original Primary Care Evaluation of Mental Disorders (PRIME-MD) (Kroenke, Spitzer, & Williams, 2001) which assessed the five most common disorders in clinical populations using the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria (APA, 2000): depressive, anxiety, somatoform, alcohol, and eating disorders. The eight items in the PHQ-8 reflect the DSM-IV criteria for the diagnosis of depressive disorders. The PHQ-8 omits the ninth criterion, referring to suicidal ideation, which is in the PHQ-9. The PHQ-8 is suited for large epidemiological studies, or even some clinical and research settings, when the risk of participants endorsing this item is presumed to be extremely low and there is not the scope for the researcher to follow up high scores on a self-report

risk item. Respondents rate the frequency they experience each depressive symptom from 0 (“Not at all”) to 3 (“nearly every day”) over the last two weeks. Scores on the PHQ-8 range from 0 to 24. The same scoring criteria for depression severity can be used for both measures as deletion of the ninth item has a minimal effect on scoring in a general population sample and it is the least frequently endorsed item on the scale by far (Kroenke et al., 2002).

The original validation study for the PHQ-9 (Kroenke et al., 2001) demonstrated that it has high internal consistency (Cronbach’s α =.89) and test-retest reliability (Pearson’s r =.84) and good convergent validity (Pearson’s r =.73). A cut-off score of 10 or greater resulted in 88% sensitivity and 88% specificity, although more recent estimates suggest higher sensitivity (Gilbody, Richards, Brealey, & Hewitt, 2007). The PHQ-8 can also be scored either by using a DSM-IV diagnosis-based algorithm or by using the cut-off score of 10 or greater at a sensitivity of 100% and specificity of 95% (Kroenke et al., 2009). The PHQ-8 and PHQ-9 were found to correlate very highly (Pearson’s r=.997) across the two validation studies for the PHQ-9 totalling 6000 participants, in diagnosing clinical depression (Kroenke, Spitzer, Williams, & Lowe, 2010).

There is currently no ‘gold standard’ screening measure of postnatal depression on the basis of the measure’s sensitivity and specificity to detect postnatal depression (Ukatu, Clare, & Brulja, 2018). The Edinburgh Postnatal Depression Scale (EPDS) is the most widely used measure of postnatal depression (Kroenke et al., 2010), though the majority of studies comparing the properties of the EPDS and PHQ-9 have found them to have comparable properties in detecting perinatal depression (Bennett et al., 2008; Gjerdingen, Crow, McGovern, Miner, & Center, 2009; Weobong et al., 2009). NICE guidelines in 2007 recommended that women are first asked the ‘Whooley questions’ (two questions regarding depression symptoms) by healthcare professionals at routine perinatal appointments and that either the EPDS, the HADS (Hospital Anxiety and Depression Scale) or PHQ-9 (Patient Health Questionnaire – 9) could be used as follow-up self-report measures to support further assessment of depression when needed (NICE, 2007).

Generalised Anxiety Disorder (GAD-7).

The GAD-7 is a seven-item scale that is widely used to screen for anxiety disorders in primary care populations (e.g., IAPT, United Kingdom). The GAD-7 was developed following on from the popularity of the PHQ-9 and was based on a similar response set (Kroenke et al., 2010). The seven items relate to the DSM-IV symptom criteria for Generalised Anxiety Disorder and respondents rate the frequency they experience each anxiety symptom over the last two weeks on the same four point scale as the PHQ-8, ranging from 0 ("Not at all") to 3 ("nearly every day"). Scores range from 0 – 21. The GAD-7 was originally validated in a primary care population to identify cases of Generalised Anxiety Disorder (GAD) with a sensitivity of 89% and specificity of 82% at a cut-off score of 10 or greater (Spitzer, Kroenke, Williams, & Lowe, 2006). The GAD-7 has high internal consistency (α = .92) and test-retest reliability (*r* = .83). The measure has good convergent validity with high correlations with other measures of anxiety (Beck Anxiety Inventory, *r* = 0.72; anxiety subscale of the Symptom Checklist-90, *r* = .74). GAD-7 severity is associated with worsening function, as measured by the Short-Form General Health Survey (SF-20). The GAD-7's ability to detect anxiety disorders other than GAD (e.g., social phobia, panic disorder and post-traumatic stress disorder) has also been established with good sensitivity and specificity (although lower than for GAD specifically) at a cut-off point of 8 or greater (Kroenke, Spitzer, Williams, Monahan & Lowe, 2007) , which is the cut-off point adopted by IAPT. The GAD-7 is increasingly being used as a screening measure of non-specific anxiety in primary care clinical practice (Clark et al., 2009).

Comorbidity with depression is well-established in the perinatal population as it is in the general population (Grigoriadis et al., 2011; Reck et al., 2008; Wenzel et al., 2005); however, the GAD-7 retains its clinical utility in differential diagnosis (Kroenke et al., 2010). Factor analysis with the PHQ-8 and GAD-7 together has confirmed that the depression and anxiety items fall on two distinct dimensions (Kroenke et al., 2010).

Perinatal anxiety has been measured by a variety of validated self-report measures in the literature including the Hospital Anxiety and Depression Scales (Zigmond & Snaith, 1983), State-Trait Anxiety Inventory (Spielberger, Gorsuch, & Lushene, 1970), General Health Questionnaire (Goldberg & Hillier, 1979) and the GAD-7 (Spitzer et al., 2006). The GAD-7 has been validated in a perinatal

psychiatric population (Simpson, Glazer, Michalski, Steiner, & Frey, 2014) and amongst pregnant Peruvian women (Zhong et al., 2015) and found to have acceptable reliability, concurrent validity, specificity and sensitivity. Further validation in large community perinatal samples is warranted; however, the GAD-7 sufficiently captures the symptomatology of anxiety disorders in the perinatal population and allows comparison with the general population (Misri et al., 2015).

Patient Health Questionnaire-15 (PHQ-15).

Despite the recognition that somatic symptoms are valid indicators of poor emotional wellbeing during the perinatal period (Senturk et al., 2012), somatic symptoms may have remained an under-researched area of perinatal distress due to difficulties in differentiating between normal somatic symptoms relating to pregnancy and the early postnatal period from somatic symptoms of distress (Wilkie et al., 2018). No measure of somatic symptoms has been consistently used within perinatal population research but the PHQ-15 has been used in perinatal mental health research (Kelly et al., 2001; Senturk et al., 2012) and demonstrated validity and reliability for assessing somatic symptoms postnatally (Wilkie, Crawley, Button, Thornton, & Ayers, 2018). Some researchers have excluded the item regarding menstruation ("how much have you been bothered by menstrual cramps or other problems with your periods") because it is less relevant during pregnancy and immediately after childbirth (Kelly et al., 2001; Senturk et al., 2012).

The PHQ-15 has several strengths as a measure of somatic symptom severity. First, the PHQ-15 consists of 15 somatic symptoms from the self-administered version of the PRIME-MD diagnostic instrument (see above) which is based on DSM-IV criteria for somatic symptom disorders (previously known as somatoform disorders). Secondly, the PHQ-15 is widely used in various healthcare settings as a screening tool for somatic symptom disorders in the general population and contains items that relate to the most common physical symptoms that patients present in primary care settings in high-income countries (Kroenke et al., 2010). Third, the PHQ-15 was validated in both primary care and obstetrics–gynecology samples in the original validation study (Kroenke et al., 2002).

The PHQ-15 does not differentiate between medically unexplained symptoms and symptoms with biological bases. Respondents are asked to rate the presence and severity of symptoms in the last four weeks on a scale from 0 ("not at

all") to 2 ("bothered a lot"). The total score ranges from 0 to 30 and, similar to the PHQ-8, cut-off scores of 10 or greater can be used to indicate the presence of moderate somatic symptom severity. The original validation study demonstrated excellent internal reliability ($\alpha = .90$) and convergent reliability demonstrated by significant pairwise comparisons ($p<.001$) between PHQ-15 levels of severity and worsening function on the SF-20 as well as levels of health care use (Kroenke et al., 2002). It has proven discriminant validity as evidenced by the differential effects of somatic symptoms (PHQ-15) and depressive symptoms (PHQ-9) on various health outcomes (Kroenke et al., 2002). More recently, an algorithm specifying three or more symptoms rated at "bothered a lot" in the last 4 weeks identified a DSM-IV somatoform diagnosis with 78% sensitivity and 71% specificity (van Ravesteijn et al., 2009).

For the purposes of this study, the term 'somatic symptoms' refers to all somatic complaints identified by the PHQ-15, whether or not they have been demonstrated to be medically unexplained.

List of Threatening Life Experiences Questionnaire (LTE-Q).

The LTE-Q (Brugha et al., 1985) is a twelve-item checklist of common adverse life events that are likely to have considerable long-term threat including events in the areas of health, marital and social relationships, bereavement, work and financial. The LTE-Q assesses life adversity over the past 6 months (rated dichotomously as yes/no). Women in the BaBY study were additionally asked to provide the date (day/month/year) of any life event experienced.

The LTE-Q is a brief, self-report measure and has an advantage in large studies over more in-depth life event interviews such as the Life Events and Difficulties Schedule (LEDS) which requires training and is time-intensive. The LTE-Q is well suited to large studies because it can be easily administered at multiple time-points. Moreover, the LTE-Q has been shown to capture 82.5% of the life events elicited in the LEDS (Brugha et al., 1985), although more recent estimates suggest a lower proportion when the reporting period is extended to 12 months (Donoghue et al). The LTE-Q has excellent test-retest reliability ($\kappa = 0.78$-1.0 for all items, except "Something you valued was lost or stolen" which was $\kappa = 0.24$) and good agreement with interview-based ratings with high sensitivity (89%) and specificity (74%) for events 6 months prior to data collection (Brugha & Cragg,

1990. No measure of stressful life events has been consistently used within perinatal research, however, the LTE-Q has been used in recent perinatal depression studies (Agostini et al., 2015; Bisetegn, Mihretie, & Muche, 2016; Pingo, van den Heuvel, Vythylingum, & Seedat, 2017; Reid, Power, & Cheshire, 2009).

Frequency of data collection

Life events (LTE-Q), depression (PHQ-8), anxiety (GAD-7) and somatising (PHQ-15) were measured at the three time-points in the study: 26 weeks pregnancy, 8 weeks postnatal and 1 year postnatal. As shown in Figure 1, the LTE-Q assessed life events in the preceding 6 months at each data collection point as indicated by the arrows. The timing of assessment in the present study means that life events collected at eight weeks postnatal for the past six months has a four week overlap with life events captured at 26 weeks pregnancy. Moreover, there was a period of 18 weeks in between life event assessment at 8 weeks postnatal and 1 year postnatal where life events occurring was not assessed.

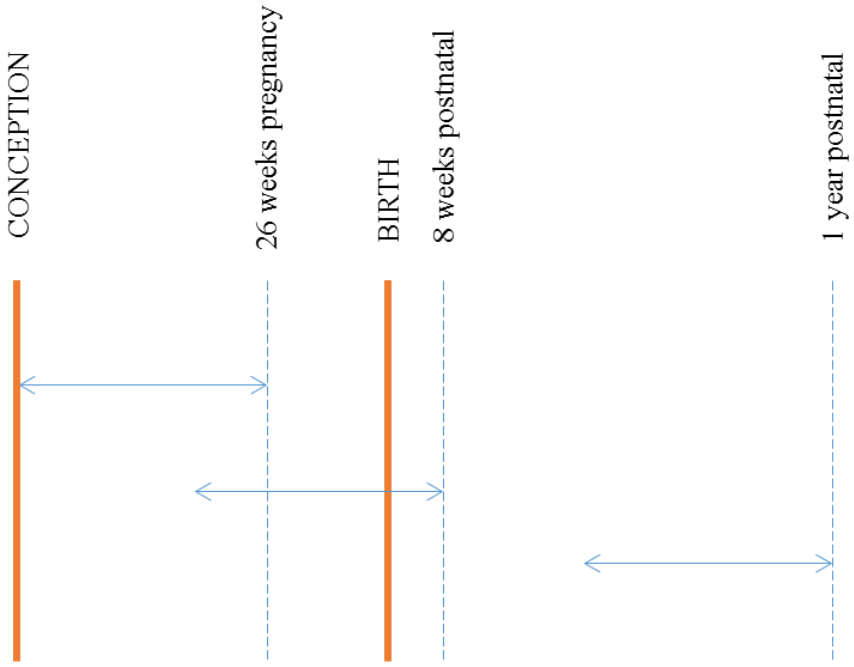

Figure 1. Timeline of life event assessment

Variables

Outcome variable.

The primary outcome of interest was depression symptoms in the perinatal period. Depression status was dichotomised as either depressed or non-depressed in the analysis using the recommended cut-off of a score of 10 or greater on the PHQ-8 to indicate depression symptoms that are likely to be of at least moderate clinical severity (Kroenke & Spitzer, 2002). Dichotomising continuous data is associated with a reduction in statistical power because of the loss of information; however, it is still common in clinical research because it is often useful to interpret results in light of diagnostic and treatment implications which may rely on categorical descriptions (Altman & Royston, 2006).

However, the cut-point needs careful consideration. Inevitably, there will be cases of sub-clinical or mild depression symptoms in the "non-depressed" group by virtue of being below the cut-off for moderate depression symptoms. However, it has recently been demonstrated that the prevalence of mild depression symptoms (PHQ-8 scores 5–9), as opposed to moderate, may be elevated in pregnant women over the general population because of a greater endorsement of somatic symptoms in the scale that can be caused by both depression and pregnancy (McMahon et al., 2017). Moderate depression symptoms (PHQ-8 ≥10) on a depression screening measure are less likely to be due to normal pregnancy-related somatic symptoms alone.

Importantly, the National Institute for Health and Care Excellence (NICE) stepped care model for treatment of depression symptoms that are below the clinical cut-off in primary care (e.g., IAPT) is "watchful waiting" and self-help (Arroll, Moir, & Kendrick, 2017). In these cases, the GP will often review self-reported depression symptoms again at a two week follow-up given that a number of people recover from symptoms of mild distress without intervention (Posternak & Miller, 2001). On the other hand, patients with moderate depression symptoms (e.g., PHQ-9 ≥10) or with persistent sub-clinical depression are offered antidepressants or a high-intensity psychological intervention, such as Cognitive Behavioural Therapy (CBT). Therefore, it is especially important to detect depression symptoms in perinatal women that are of a severity where they are less likely to dissipate over time and would warrant a change in patient care.

Cross-sectional analyses.

Depression status (depressed versus non-depressed) was used as the outcome variable in cross-sectional analyses of the relationship between life events and depression at the three time-points in the perinatal period: 26 weeks pregnancy, 8 weeks postnatal, and 1 year postnatal.

Prospective analyses.

A prospective examination of the relationship between life events and depression means that life events can be explored as a predictor of new cases of postnatal depression onset (in the absence of depression at 26 weeks pregnancy). However, reported rates of postnatal depression onset in the literature (e.g., 6.5%, Gavin et al., 2005) have generally been lower than point-prevalence estimates of postnatal depression at a given time.

Therefore, it was intended that postnatal depression onset would be used as the outcome variable if there were sufficient numbers in the complete case sample (see description in *Data Preparation* below) for a sufficiently powered analysis model. However, if the prevalence of postnatal depression onset was too low, the prevalence of depression at any time during the postnatal period would be used as the outcome variable whilst adjusting for the presence of antenatal (baseline) depression at 26 weeks pregnancy.

Similarly, it was intended that the relationship between life events during pregnancy and postnatal depression would be examined separately at 8 weeks postnatal and 1 year postnatal if there were sufficient numbers of postnatal depression in the final complete case sample in order to identify any differences in association between life events during pregnancy and depression at 8 weeks and 1 year postnatal.

Exposure variable.

The number and type of life events were explored as separate predictors of perinatal depression in the cross-sectional and prospective analyses.

Number of life events.

The number of life events as a predictor for perinatal depression has been explored both using the total score (as a continuous variable) and categories of frequency such as 0, 1 or 2 or more life events (dichotomous or ordinal variables) in the literature (e.g., Verreault et al., 2014, Holzman et al., 2006, Shakeel et al., 2015). Several studies have found that life events as a dichotomous variable is more appropriate where the number of life events reported by participants is heavily negatively skewed (e.g., few reporting more than two negative life events) (Donoghue et al., 2016; Keers et al., 2010). The number of life events reported in perinatal samples varies depending on the specific population and life events measure used. Therefore, the numbers reported in the final sample (see description in *Data Preparation*, below) were considered in the decision regarding the most appropriate predictor of life events frequency. It was intended that, if the total score did not have enough variation to assess a dose-response relationship with depression, then the dichotomous outcome would be used to assess whether the experience of one or more life events increases the risk of experiencing depression relative to no life events.

Type of life events.

Each of the 12 items on the LTE-Q were investigated individually for their association with perinatal depression.

Covariates.

Minimal biographic and demographic data were available from the BaBY study: age and postcode. The Index of Multiple Deprivation Decile Rank was derived for each participant from their postcodes using a UK government online tool "Postcode Lookup" (http://imd-by-postcode.opendatacommunities.org/) based on the latest English Index of Multiple Deprivation (IMD) 2015 data (Department for Communities and Local Government, 2015). Each woman was assigned a decile rank between one and ten which served as a proxy for deprivation level in this study. The IMD decile rank is commonly used to describe how relatively deprived a small area in England is, with one representing the ten percent most deprived and ten representing the ten percent least deprived. Research has demonstrated that both the youngest and oldest mothers of child-bearing age are at a higher risk of experiencing

perinatal depression (Biaggi et al., 2016). Therefore, age was entered as a four-level categorical predictor (≤20, 21-30, 31-40, 41-50 years) which allows each age bracket to have a unique relationship with depression risk. The middle group (31-40 years old) was chosen as the reference category so that it could demonstrate any elevated risk at the two extreme ends of the age spectrum (Katz, 2011). Deprivation was entered as a continuous score (1-10).

Concurrent anxiety and somatic symptoms were entered in the cross-sectional models throughout the perinatal period, whilst antenatal anxiety and somatic symptoms were entered in the prospective models. Similarly to depression, anxiety and somatic symptoms were dichotomised using clinical cut-off scores commonly used in primary healthcare to indicate a moderate severity of symptoms (Kroenke et al., 2010). Anxiety symptoms were defined as scores of 8 or more on the GAD-7, and somatic symptoms were defined as scores of 10 or more on the PHQ-15. The discussion above regarding the benefits and costs of dichotomising variables is also relevant to the decision to dichotomise anxiety and somatic symptoms in this study. The NICE stepped-care model applies to both subclinical mild-to-moderate depression and anxiety symptoms (NICE, 2011). In addition, there is an expected increase in somatic symptoms during pregnancy because of pregnancy-related physical changes (Simpson et al., 2014). Therefore, using the cut-off for a moderate severity of somatic symptoms will go some way towards addressing this response bias.

Data preparation

Data quality check.

Data from the paper copies of questionnaires completed by the women were entered manually into an electronic database by members of the BaBY research team. The source data verification procedure (Houston, Probst, & Martin, 2018) for ascertaining data quality of the electronic data was carried out by conducting a random 10% sample check of cases at each of the three time-points in the study: 26 weeks pregnancy (N = 207), 8 weeks postnatal (N = 176), and 1 year postnatal (N = 124). Data recorded in the database for these participants was checked against the paper copies of the questionnaires which were kept in locked cabinets at the University of York. The error rates were 0.48% at 26 weeks pregnancy, 2.84% at 8

weeks postnatal, and 0% at 1 year postnatal. The error rates were within acceptable limits (<5%) and, therefore, data were considered to be of reasonably high quality and no further random sampling was necessary.

Complete case sample.

The study aimed to examine the prospective association between life events during pregnancy and postnatal depression whilst controlling for the effects of other demographic and clinical risk factors. However, there was missing data across time points in the study presumed to be a result of participant non-response and some participants joining at later time points in the study. Regression models are highly flexible in modelling outcomes with a variety of predictors and covariates (independent variables) but they also require all observations to have complete data in every variable in order to be included in the model (Katz, 2011). This means that any cases which do not have complete data at every time point would be dropped from the regression model. Therefore, we specified that only cases which had complete data at all three time-points (i.e. a score was generated for each questionnaire at each time-point) were retained for analysis. As a result, there was continuity across all models regarding the number and characteristics of the sample which enabled comparisons between models.

Inverse probability weighting and multiple imputation were considered as alternatives to creating a complete case sample. Inverse probability weighting and multiple imputation are more complex methods of dealing with missing data that rely on using extensive pre-existing information on the non-responders to create 'plausible missing data' based on similar participants in the sample who did respond (Seaman & White, 2013). In this study, extensive pre-existing information was not available regarding the non-responders in the sample and, therefore, it was not possible to generate unbiased imputed data.

Incorrect or missing data in the complete case sample.

Outliers.

The data were screened for outliers using descriptive and graphical methods of representing the data (means, standard deviations, minimum and maximum values, histograms, stem-and-leaf plots). Several high LTE-Q scores were identified

(a score of 12 out of a maximum score of 12) that clearly stood out from the distribution of the rest of the data and did not have any accompanying dates of the events. The paper copies were obtained to rule out data entry errors. On the basis that it is very unlikely that someone would experience 12 life events in a 6 month period as well as not provide any dates for the events, it was assumed that the participants had intended to tick 'no' instead of 'yes' to these life events. Therefore, the life events data were corrected for these cases. See Appendix F for full description on all data corrections and exclusions.

Demographics.

Incorrect or missing postcodes were double-checked with the BaBY research team and recovered by reviewing the original consent forms. Missing ages were identified in the same process.

PHQ-15: menstruation item.

Previous studies have tended to exclude the item regarding problems with menstruation when examining the pregnancy period as it is not relevant and the PHQ-15 does not have a 'not applicable' option (Kelly et al., 2001; Senturk et al., 2012). The item was retained in the present study because the study period spans pregnancy and the postnatal period up to 1 year and menstruation is expected to return around 8 weeks postnatal in the absence of breastfeeding (Visness & Kennedy, 1997). Therefore, in the present study, all responses to the item at 26 weeks pregnancy were recoded "not at all" (0), and any missing items at 8 weeks postnatal or 1 year postnatal were recoded to "not at all" (0). It was assumed that the menstruation item was missed by women in the postnatal period who were still breastfeeding or had become pregnant again at 1 year postnatal and, therefore, was not relevant to them. It is worth noting that the UK prevalence of mothers still breastfeeding at 1 year postnatal is estimated as less than one percent (Lancet report). A slightly higher proportion of women in the present study sample had missing data for this item at 1 year postnatal (three percent). However, anecdotal evidence from the BaBY research team suggested that a number of women reported being pregnant at the 1 year follow-up.

Life event dates.

Women were asked to report the dates (day/month/year) of any life events experienced. Therefore, it was possible to check the data quality of the life events to make sure that they were within the six month period specified on the questionnaire. 6% of women (N = 56) reported life events (168 in total) that were outside the specified six-month period. These specific events were deleted from the dataset and replaced with a '0' (no life event) for that life event. This did not alter the complete case sample. Any life events that did not have corresponding dates reported for them (88 in total) were kept in the dataset because it was assumed that they were more likely to be in the specified period than not.

Missing data within measures.

Missing items within the PHQ-8, GAD-7 and PHQ-15 were replaced with the mean score of the completed items, provided that the number of missing items did not exceed 20% of the total items (Kroenke et al., 2010). In line with previous research, missing items in the LTE-Q were recoded as 'No' (scored as 0) provided there was only one item missing (Donoghue et al., 2016). It was assumed that people would complete any memorable events if they had occurred. See Appendix F for full description on all data corrections and exclusions.

Data analysis

Data were analysed using Stata version 14 (StataCorp, 2015). Initially, the data were explored using descriptive statistics (means, standard deviations, minimum and maximum values), histograms, stem and leaf plots and estimates of skewness in order to examine the distribution of the data and identify outliers. To investigate the distribution of age and deprivation profiles, the mean scores, standard deviations and the proportion of the sample in specific age and deprivation brackets were examined. Similarly, mean scores and standard deviations were calculated for depression, anxiety and somatic symptoms, as well as the proportion of the sample scoring above the clinical cut-off values. Life event data was also analysed to show the percentage frequencies of life events reported and the types of life events (individual responses to the LTE-Q items). These clinical and demographic data were calculated for the overall sample and then by depression status (depressed versus non-depressed) across the three time-points in the study. The prevalence of

depression, anxiety and somatic symptoms (above the clinical cut-off), as well as the rate of onset of symptoms (defined as a change in score from below to above the clinical cut-off from one time-point to the next) were established using frequency count and percentages. The proportion of women changing in "caseness" (whether symptoms are above the clinical cut-off) in depression, anxiety and somatic symptoms from one time-point to the next over the perinatal period was also calculated.

The complete and incomplete cases were tested for significant differences on baseline (26 weeks pregnancy) demographic and clinical characteristics. For continuous variables such as age and deprivation, *t*-test for independent samples was used for data with parametric distributions and equal variances, and the Mann Whitney U test was used for those with non-normal distributions with unequal variances. Pearson's Chi-square test was used to test for categorical differences in the proportions of the sample above clinical cut-offs on anxiety and somatic symptoms between depressed and non-depressed groups.

Similarly, the depressed and non-depressed groups in the complete case sample were compared on their clinical and demographic characteristics at all three time-points using *t*-test for independent samples, Mann Whitney U tests and Pearson's Chi-square test, as appropriate. Differences between the depressed and non-depressed groups on individual life event items were examined using Fisher's exact tests. Fisher's exact test is the recommended alternative to Chi-square test for cell counts less than five in a cross-tabulation of the variables (Katz, 2011).

Multivariable logistic regression models.

The association between life events and depression across the perinatal period was analysed using a series of cross-sectional and prospective multivariable logistic regression models. Logistic regression is used when modelling a binary outcome, as in the case of the present study which focuses on depressed versus non-depressed status (Tabachnick & Fidell, 2013). Several longitudinal studies have explored the relationship between life events and perinatal depression using a combination of univariable and multivariable regression techniques, including logistic regression (see Leigh & Milgrom, 2008; Milgrom et al., 2008; Rubertsson et al., 2005). Multivariable logistic regression allows for the examination of unique association between life events and perinatal depression, whilst controlling for a

number of demographic and clinical variables. Logistic regression is a useful statistical technique within clinical health research as it produces an effect-size statistic that gives clear information to both clinicians and patients about the size of effect treatments or exposures have on the odds of a clinical outcome (Katz, 2011).

Cross-sectional analyses.

In the cross-sectional analyses, the association between the number and type of life events and concurrent depression symptoms was explored at each of the three time-points in the study (26 weeks pregnancy, 8 weeks postnatal, and 1 year postnatal). Three logistic regression models were constructed at each time-point. The first model was a univariable, unadjusted model exploring the association between life events and perinatal depression. The life events frequency predictor was entered in this first stage. The life events type predictor was determined at each time-point by first examining each of the 12 life event types in univariable logistic regression models for their association with depression. Only significant life events (p <.05) from this stage were carried forward into the multivariable adjusted models. This method is the recommended strategy when the relative importance of independent variables in a set are unknown because it ensures that as few independent variables are included in a model as possible (Katz, 2011; Tabacknick & Fidell, 2013). The second model additionally adjusted for demographic variables which were entered into the model simultaneously: age (examined as a categorical variable) and deprivation level (examined as a continuous variable). The third model further adjusted for other clinical predictors using simultaneous entry of anxiety and somatic symptoms (examined as dichotomous variables).

Prospective analyses.

In the prospective analyses, the aim was to investigate life events occurring during pregnancy as predictors of postnatal depression. Life events during pregnancy were assessed at two time-points in the study: at 26 weeks pregnancy (covering life events from conception to mid-pregnancy) and at 8 weeks postnatal (covering life events from mid-pregnancy to the first 8 weeks post-delivery (see Figure 1). Due to the timing of life event assessment in this study, it was not possible to obtain an estimate of life events occurring solely during pregnancy and up until the point of delivery as the second assessment point included the early

postnatal period. Therefore, life events occurring during pregnancy as a predictor of postnatal depression (at 8 weeks and 1 year postnatal) was examined in two ways: first, life events in the early to mid-pregnancy period (assessed at 26 weeks pregnancy); and secondly, life events in the mid-pregnancy to early postnatal period (assessed at 8 weeks postnatal).

Interpretation.

Logistic regression calculates the odds ratio (OR) which is a measure of association between an exposure and an outcome (Szumilas, 2010). The OR is the ratio of the odds of an outcome occurring (e.g., depression) when a given exposure is present (e.g., life events), compared to the odds of the outcome occurring when the exposure is absent (Tabacknick & Fidell, 2013). Predictor (exposure) variables can be continuous or categorical. ORs range between 0 and infinity and are often interpreted as percentages. An OR greater than 1 indicates that the outcome is more likely to happen than not, whereas an OR of less than 1 indicates that it is less likely to happen. If the OR equals 1, then the exposure has no effect on the odds of the outcome. The 95% confidence intervals (CI) for the OR indicate the relative precision of the estimate with a wider CI indicating less precision. The *p* value for an OR indicates whether the effect is statistically significant, but the CI is often reported as a proxy for statistical significance (Szumilas, 2010). CI for OR that cross 1 indicate that the predictor variable could have a positive effect, negative effect or no effect (a value of 1) on the outcome and, therefore, cannot be a significant predictor. The Likelihood ratio test (the model chi-square) was conducted for each multivariable regression model to determine whether the full model with its set of predictors is a significantly better predictor of the outcome than a model with no predictors (i.e. a constant-only model) (Katz, 2011). A small *p* value ($p < .05$) indicates that the full model is significantly better than the constant-only model.

Assumptions.

Binary logistic regression requires the outcome variable to be binary (two categories). Logistic regression does not require the usual assumptions of linear regression which assume linearity between dependent and independent variables, normality of residuals and homoscedasticity (Tabachnick & Fidell, 2013). However, logistic regression assumes that there is linearity between continuous independent

variables and the log odds (Katz, 2011). This assumption is tested by entering an interaction term between the continuous independent variable and its log transformation into the regression model and testing for significance. Independent variables should also have little to no multicollinearity between them, that is, they should not be too highly correlated with each other. This can be ascertained using test statistics that produce tolerance and variance inflation factor (VIF) values, with tolerance values greater than 0.1 and VIF values less than 10 indicating the absence of multicollinearity (Katz, 2011). Logistic regression also requires sufficiently large samples sizes to produce unbiased estimates. A typical guideline is that there should be at least 10 cases in the least frequent outcome for every independent variable in the model (Katz, 2011).

To indicate how well each model is specified, post-estimation tests were performed after running each regression model. In logistic regression, the Hosmer-Lemeshow goodness-of-fit test assesses how similar the estimated probability in the model is to the observed probability of the outcome (Katz, 2011). A good model fit is indicated by a non-significant *p* value (i.e. the estimated model is not significantly different from the observed model). Residual statistics (standardised residuals, leverage, deviance residuals) were used to examine whether any observations were having an excessive influence on the model and introducing bias (Katz, 2011). Standardised residuals greater than 2 to 3 are indicative of observations that represent observations at the extreme end of the distribution (Katz, 2011).

Sample size in the present study

A power calculation to determine the sample size needed to detect an effect at a reasonable power level requires information about the expected prevalence of the outcome in a population (e.g., prevalence of perinatal depression) and the estimated effect size of the exposure (e.g., effect size of life events) (Katz, 2011). For this study, it is not assumed that either the true estimates of the prevalence of perinatal depression or the effect size of life events on perinatal depression are currently known in the literature. Furthermore, this study is conducting secondary data analysis on data that has already been collected as part of the BaBY study. Therefore, an *a priori* sample size calculation was not conducted. Instead, the observed prevalence of depression symptoms in this study was used in post-hoc estimations to calculate the minimum sample size needed in a logistic regression

model. Peduzzi, Concato, Kemper, Holford, and Feinstein (1996) suggest that a conservative estimate of the sample size needed in a logistic regression model is:

$$10 \times (k/p)$$

where k = the number of predictors (independent variables) in the model and p = the prevalence of the outcome in the sample. The results of the post-hoc estimated sample size are reported in the *Results* chapter.

Ethical considerations

Ethical clearance.

Clearance to conduct secondary analysis of data collected through the BaBY study was subsumed within the original ethical approval from the North East – York Research Ethics Committee (11/NE/0022). A copy of the REC approval letter can be found in Appendix A. In addition, the present study was reviewed and approved by the BaBY trial management group.

Data storage.

Mental wellbeing and life events data from the self-report questionnaires were entered into a secure database located in the Department of Health Sciences at the University of York by members of the BaBY research team. All paper copies of questionnaires or consent forms were kept separately in locked cabinets at the University of York. Anonymised data for analysis in this study were transferred via the secure University of York DropOff service which encrypts the data and can only be downloaded with a specific password. The data were downloaded to the University of Leeds N: drive by research staff on the Doctorate of Clinical Psychology Programme which is a secure network server. Only named individuals have access to the password-protected files.

Results

This chapter presents and explores the results from this study. First, the process of obtaining a complete case sample for multivariable analysis is described and the differences between the complete and incomplete samples on baseline (26 weeks pregnancy) maternal characteristics are compared. Second, the point-prevalence estimates of self-reported depression, anxiety and somatic symptoms is described across the perinatal period and the incidence of postnatal depression (rate of new cases) for the complete case sample. Third, descriptive results comparing the depressed and non-depressed groups of women on demographic and psychosocial variables across the perinatal period is reported. Finally, the association between the number and type of life events experienced and depression in the perinatal period is explored. This is done in two stages: first, the association between life events and the prevalence of depression is explored cross-sectionally during pregnancy and in the first postnatal year; secondly, prospective associations between life events during pregnancy and the early postnatal period and the presence of postnatal depression are explored. This as achieved using a series of univariable and multivariable logistic regression models that examine the unique association between life events and perinatal depression whilst controlling for selected demographic variables, as well as, levels of anxiety and somatising symptoms.

The aims of these analyses link directly to the overall aims of the study (see *Introduction* chapter) and were as follows:

1. To establish the levels of self-report depression, anxiety and somatic symptoms in a large, non-clinical population of mothers during pregnancy and in the first postnatal year.

2. To examine the association between the number and type of life events experienced and depression (whilst controlling for demographic variables, levels of anxiety and somatic symptoms) in a series of cross-sectional and prospective regression models.

The second aim was achieved through the following specific objectives to investigate:

i. Cross-sectional associations between life events and the prevalence of depression at three time-points during the perinatal period (26 weeks pregnancy, 8 weeks postnatally, 1 year postnatally).
ii. Prospective associations between life events occurring during pregnancy and the early postnatal period and postnatal depression, with one model including early to mid-pregnancy and a second, mid-pregnancy to the early postnatal period.

Participants

Sample size – complete cases available for analysis.

A total of 4164 women consented to take part in the BaBY study, of which 2382 women returned at least one mental wellbeing or life event questionnaire, yielding a crude response rate of 57.2%. In order to prevent cases being dropped from the logistic regression analyses (because of missing values), it was necessary to obtain a complete case sample that had no missing data. Therefore, cases were excluded if they did not have complete mental wellbeing and life events data at all three time-points in the study (see Figure 2). The limitations of this in terms of bias are considered in the final chapter. A total of 917 cases were retained, yielding an adjusted response rate of 22.0% and a retention rate across the study time-points of 45.8%. Data cleaning resulted in a further ten cases being excluded, leaving 907 complete cases for analysis. Nine of these ten cases were excluded due to unacceptable levels of missing item data within one of the questionnaires (see *Missing data within measures*, *Method* chapter) and one case was excluded with a high LTE-Q score (10 out of a maximum score of 12) because it was not possible to determine from the pattern of life events and dates reported what the errors were, and the high score would likely have a large influence on the analysis model. See Appendix F for full description on all data corrections and exclusions.

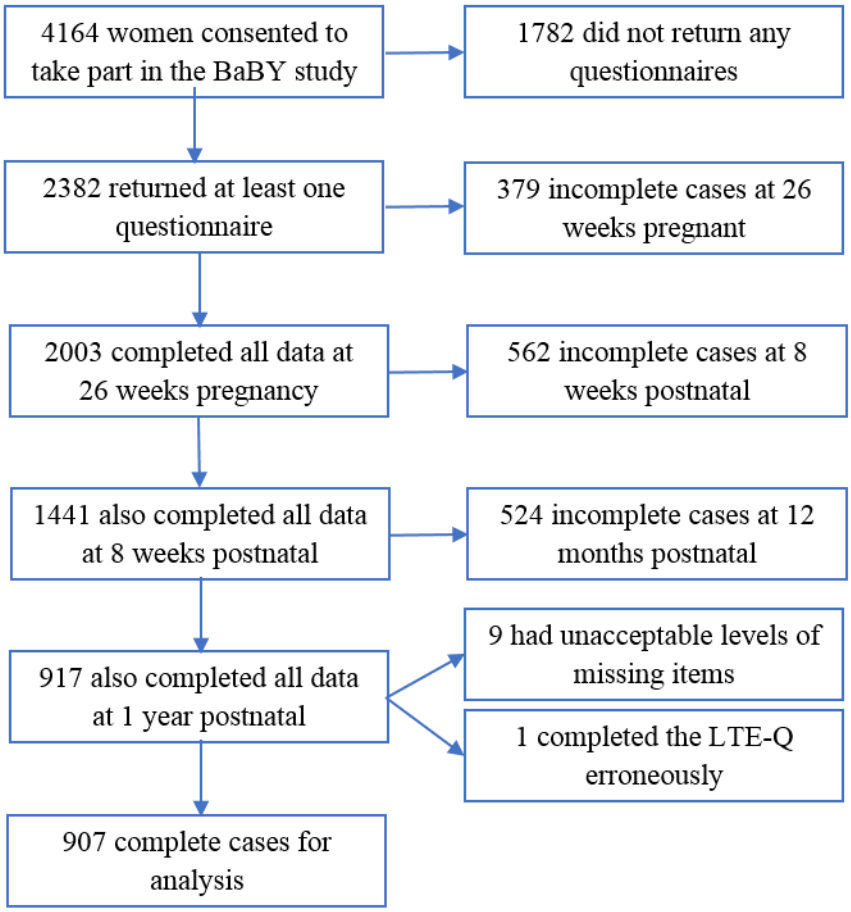

Figure 2. Flowchart illustrating the process of obtaining a complete case sample

Characteristics of the complete versus incomplete sample.

Baseline characteristics of the complete and incomplete samples at 26 weeks pregnancy were examined to determine whether they were significantly different (see Table 2). The incomplete sample consisted of all the cases which had one or more questionnaires missing (N = 1465). After data cleaning, ten cases were dropped from the incomplete sample because of unacceptable levels of missing items within the questionnaire, leaving 1455 women who returned at least demographic data at 26 weeks pregnancy. Not all of these women returned every questionnaire at 26 weeks pregnancy (see Table 2, legend). Differences between the two samples were explored using *t* tests for independent samples, Chi-square test and Mann Whitney U tests as appropriate to account for non-parametric and unequal variance distributions in the data.

Significant differences were observed between the two groups on all variables (Table 2). The data in Table 2 indicate that, compared to the complete cases, younger women, from marginally more deprived backgrounds presenting with higher symptoms of distress during pregnancy and a higher number of life events were less likely to continue to participate for the duration of the study. Hereafter, the results in this chapter are drawn from the complete case sample only.

Table 2. Characteristics of the complete and incomplete sample at baseline

Characteristics at baseline (26 weeks pregnancy)	**Complete (*N* = 907)**	**Incomplete (max. *N* = 1455)†**	***p* value**
Age (years), mean (SD)	32.0 (4.79)	30.0 (5.42)	<0.001[a]
Index of Multiple Deprivation Decile, mean (SD)	7.4 (2.36)	6.6 (2.74)	<0.001[c]
Depression symptoms, %	7.3	11.7	0.001[b]
Anxiety symptoms, %	9.5	15.7	<0.001[b]
Somatic symptoms, %	26.2	31.9	0.040[b]
Life events (total), mean (SD)	0.3 (0.70)	0.5 (0.89)	0.019[c]

Note: Depression symptoms were defined as scores on the PHQ-8 ≥10. Anxiety symptoms were defined as scores on the GAD-7 ≥ 8. Somatic symptoms were defined as scores on the PHQ-15 ≥10. Deciles range from 1 (most deprived) to 10 (least deprived).
†Age, index of multiple deprivation (*N* = 1455), depression symptoms (*N* = 1134), anxiety symptoms (*N* = 1099), somatic symptoms, life events (*N* = 1089).
[a] *p* values were derived from *t*-tests for independent samples.
[b] *p* values were derived from Pearson's Chi-square tests.
[c] *p* values were derived from Mann-Whitney U tests.

Characteristics of the complete sample across the perinatal period

Characteristics of depressed and non-depressed women in the complete sample.

Table 3 provides details of the characteristics of depressed and non-depressed women across the perinatal period. Pearson's Chi-square, *t*-test for independent samples and Mann Whitney U tests were used as appropriate to explore differences between the depressed (PHQ-8 ≥10) and non-depressed (PHQ-8 <10) women on demographics and mental wellbeing and life event characteristics.

There were no significant differences between the mean ages of women in the depressed and non-depressed groups over the perinatal period. However, there was a greater proportion of depressed women under 20 and over 40 years old which reached statistical significance at 26 weeks pregnancy (χ^2 (3) = 10.02, $p < .05$) and 8

weeks postnatal (χ^2 (3) = 8.7, p <. 05). Two thirds of the overall sample lived in the top 40% least deprived areas in England (deciles 7 – 10). However, a greater proportion of women in the depressed group tended to live in more deprived areas (deciles 1 – 4), although this only reached statistical significance at 1 year postnatal (χ^2 (4) = 13.3, p <. 05).

The depressed group had significantly higher mean scores on anxiety and were significantly more likely to have anxiety symptoms (GAD-7 score ≥8) than the non-depressed group throughout the perinatal period. During pregnancy, 60.6% of depressed women experienced comorbid anxiety symptoms, as did 71.0-75.6% of depressed women in the postnatal period. The prevalence of depression with comorbid anxiety in the overall sample was 4.4% (N = 40) at 26 weeks pregnancy, 3.8% (N = 34) at 8 weeks postnatal, and 4.9% (N = 44) at 1 year postnatal (data not shown in Table 3). Similarly, the depressed group had significantly higher mean scores of somatic symptoms and were significantly more likely to have somatic symptoms (PHQ-15 score ≥10) than the non-depressed group throughout the perinatal period. During pregnancy, 81.8% of depressed women experienced comorbid somatic symptoms, as did 51.1-58.1% of depressed women in the postnatal period. The prevalence of depression with comorbid somatic symptoms in the overall sample was 6.0% (N = 54) during pregnancy, 2.5% (N = 23) at 8 weeks postnatal and 4.0% (N = 36) at 1 year postnatal (data not shown in Table 3).

Relatively few life events were experienced in this sample: the majority of women in both the depressed and non-depressed groups across the perinatal period experienced no life events (>60%) (Table 3). Additionally, only approximately 5% of the overall sample experienced two or more life events at any time point in the perinatal period (4.7% at 26 weeks pregnancy, 5.2% at 8 weeks postnatal, 5.4% at 1 year postnatal) (data not shown in Table 2) which is reflected in the low mean scores (Table 3). However, a greater proportion of women in the depressed group experienced one or more life events and had a significantly higher mean number of life events throughout the perinatal period, compared to the non-depressed group (Table 3).

Table 3. Maternal characteristics of depressed and non-depressed women in the complete sample

Maternal characteristics	Pregnancy (26 weeks)	Pregnancy (26 weeks)			Postnatal (8 weeks)			Postnatal (1 year)		
	All (*N*=907)	Depressed (*N*=66)	Not depressed (*N*=841)	*p* value	Depressed (*N*=45)	Not depressed (*N*=862)	*p* value	Depressed (*N*=62)	Not depressed (*N*=845)	*p* value
Age (years), mean (SD)	32.0 (4.79)	32.4 (5.98)	32.0 (4.69)	0.527[a]	30.9 (6.03)	32.1 (4.71)	0.209[a]	30.9 (5.91)	32.1(4.69)	0.126[a]
Age (years), %										
≤20	1.2	3.0	1.1	0.018[b]	4.4	1.0	0.033[b]	3.2	1.1	0.267[b]
21-30	35.4	36.4	35.3		44.4	34.9		40.3	35.0	
31-40	60.1	51.5	60.8		44.4	61.0		51.6	60.7	
41-50	3.3	9.1	2.9		6.7	3.1		4.8	3.2	
IMD Deciles, mean (SD)	7.4 (2.36)	7.2 (2.78)	7.4 (2.33)	0.913[c]	7.1 (2.37)	7.4 (2.36)	0.136[c]	6.6 (2.96)	7.4 (2.30)	0.190[c]
IMD Deciles, %										
1-2	4.4	6.1	4.3	0.318[b]	4.4	4.4	0.566[b]	12.9	3.8	0.010[b]
3-4	9.0	15.2	8.6		8.9	9.1		12.9	8.8	
5-6	19.0	13.6	19.4		26.7	18.6		17.7	19.1	
7-8	25.8	22.7	26.0		28.9	25.6		22.6	26.0	
9-10	41.8	42.4	41.7		31.1	42.3		33.9	42.4	
Depression (score), mean (SD)	3.9 (3.39)	12.4 (3.10)	3.2 (2.35)		12.9 (3.12)	2.6 (2.30)		13.3 (3.63)	2.4 (2.32)	
Anxiety (score), mean (SD)	3.0 (3.52)	9.2 (4.89)	2.5 (2.87)	<.001[c]	11.7 (5.13)	2.5 (2.83)	<.001[c]	11.1 (5.46)	2.4 (2.82)	<.001[c]
Anxiety (GAD-7 ≥8), %	9.5	60.6	5.5	<.001[b]	75.6	5.6	<.001[b]	71.0	4.1	<.001[b]

Somatisation (score), mean (SD)	7.4 (3.98)	13.0 (4.08)	6.9 (3.63)	<.001[c]	9.9 (4.21)	4.3 (3.0)	<.001[c]	10.7 (4.75)	4.2 (3.22)	<.001[c]
Somatisation (PHQ-15 ≥10), %	26.2	81.8	21.2	<.001[b]	51.1	5.3	<.001[b]	58.1	8.2	<.001[b]
Life events (score), mean (SD)	0.3 (0.57)	0.4 (0.72)	0.2 (0.56)	0.038[c]	0.5 (0.69)	0.3 (0.61)	0.005[c]	0.6 (0.82)	0.3 (0.59)	0.003[c]
Life events (score), %										
0	79.6	69.7	80.4	0.007[b]	62.2	79.8	0.032[b]	61.3	77.9	0.006[b]
1	15.7	22.7	15.1		31.1	15.1		24.2	17.4	
2	4.1	4.6	4.0		4.4	4.1		11.3	3.7	
3	0.4	3.0	0.2		2.2	0.6		3.2	1.0	
4	0.2	-	0.2		-	0.5		-	0.1	
5-12	-	-	-		-	-		-	-	

Note: IMD = Index of Multiple Deprivation. Age and IMD are time-invariant, but depression, anxiety, somatising and life event scores were collected at each time-point. The depressed and not depressed groups were defined based on PHQ-8 scores: PHQ-8 ≥10 = depressed; PHQ-8 <10 = not depressed.

[a] *p* values were derived from *t*-tests for independent samples.

[b] *p* values were derived from Pearson's Chi-square tests.

[c] *p* values were derived from Mann-Whitney U tests.

Regarding specific types of life events, the three most common types of life events in the overall sample across the perinatal period were (in order of prevalence): bereavement of friends or relatives (6.7-8.9%), illness or injury in a close relative (6.6-7.1%), and serious problems with a close friend, neighbour or relative (3.0-3.9%) (Table 4). This pattern was present at all three time-points in the study. However, women in the depressed groups experienced significantly more serious financial problems at 8 weeks postnatal (Fisher's exact, $p <. 05$) and more financial problems, unemployment and breakdowns in romantic relationships at 1 year postnatal (all χ^2 and Fisher's exact tests, $p <. 05$) than the non-depressed group (Table 4). No significant differences between types of life events between the depressed and non-depressed groups were found during pregnancy.

Table 4. Life events reported by depressed and non-depressed groups of women

	Pregnancy (26 weeks)			Postnatal (8 weeks)			Postnatal (1 year)		
	All (*N*=907)	Depressed (*N*=66)	Not depressed (*N*=841)	All (*N*=907)	Depressed (*N*=45)	Not depressed (*N*=862)	All (*N*=907)	Depressed (*N*=62)	Not depressed (*N*=845)
Life events (items), *N* (%)									
You suffered a serious illness, injury or assault	12 (1.3)	2 (3.0)	10 (1.2)	24 (2.7)	3 (6.7)	21 (2.4)	5 (0.6)	0 (0.0)	5 (0.6)
A serious illness, injury or assault happened to a close relative	62 (6.8)	7 (10.6)	55 (6.5)	60 (6.6)	6 (13.3)	54 (6.3)	64 (7.1)	8 (12.9)	56 (6.6)
Your parent, child or spouse died	7 (0.8)	2 (3.0)	5 (0.6)	9 (1.0)	1 (2.2)	8 (0.9)	7 (0.8)	1 (1.6)	6 (0.7)
A close family friend or another relative (aunt, cousin, grandparent) died	70 (7.7)	2 (3.0)	68 (8.1)	76 (8.4)	3 (6.7)	73 (8.5)	81 (8.9)	6 (9.7)	75 (8.9)
You had a separation due to marital difficulties	1 (0.1)	0 (0.0)	1 (0.1)	4 (0.4)	0 (0.0)	4 (0.5)	4 (0.4)	1 (1.6)	3 (0.4)
You broke off a steady relationship	6 (0.7)	2 (3.0)	4 (0.5)	7 (0.8)	0 (0.0)	7 (0.8)	9 (1.0)	3 (4.8)	6 (0.7)*
You had a serious problem with a close friend, neighbour or relative	27 (3.0)	4 (6.1)	23 (2.7)	27 (3.0)	2 (4.4)	25 (2.9)	35 (3.9)	4 (6.5)	31 (3.7)
You became unemployed / seeking work unsuccessfully for >1 month	25 (2.8)	4 (6.1)	21 (2.5)	16 (1.8)	2 (4.4)	14 (1.6)	31 (3.4)	5 (8.1)	26 (3.1)*

You were sacked from your job	2 (0.2)	0 (0.0)	2 (0.2)	5 (0.6)	0 (0.0)	5 (0.6)	2 (0.2)	0 (0.0)	2 (0.2)
You had a major financial crisis	16 (1.8)	2 (3.0)	14 (1.7)	16 (1.8)	3 (6.7)	13 (1.5)*	22 (2.4)	6 (9.7)	16 (1.9)**
You had problems with the police and a court appearance	2 (0.2)	1 (1.5)	1 (0.1)	1 (0.1)	0 (0.0)	1 (0.1)	2 (0.2)	0 (0.0)	2 (0.2)
Something you valued was lost or stolen	3 (0.3)	0 (0.0)	3 (0.4)	7 (0.8)	1 (2.2)	6 (0.7)	10 (1.1)	1 (1.6)	9 (1.1)
Total number (*N*)	233	26	207	252	21	231	272	35	237

Note: Data in Table 4 are presented as *N* (%). Differences between depressed and non-depressed groups were derived from Pearson's Chi-square where $N > 5$ and Fisher's exact tests where $N < 5$. The depressed and not depressed groups were defined based on PHQ-8 scores: PHQ-8 ≥10 = depressed; PHQ-8 <10 = not depressed.

*significant at $p < 0.05$

**significant at $p < 0.01$

Point prevalence estimates of depression, anxiety and somatic symptoms in the perinatal period.

Figure 3 shows the point prevalence of women with self-reported depression, anxiety and somatic symptoms at each time-point in the complete case sample. The prevalence of depression in this sample remained relatively stable over the perinatal period with the highest prevalence during pregnancy (7.3%) and the lowest at 8 weeks postnatal (5.0%). The prevalence of anxiety was consistently higher than depression during the entire perinatal period and reduced marginally from pregnancy (9.5%) to 1 year postnatal (8.7%). The prevalence of somatic symptoms was considerably higher than both depression and anxiety symptoms during pregnancy and at 1 year postnatal. More than one in four women (26.2%) reported experiencing somatic symptoms during pregnancy, and approximately one in ten people (11.6%) at 1 year postnatal. However, the prevalence at 8 weeks postnatal (7.6%) was more similar to that of depression and anxiety symptoms.

Onset of depression, anxiety and somatic symptoms in the perinatal period.

Onset was defined as a change in score from below to above the clinical cut-off at the next time-point. The proportion of the sample with onset of depression symptoms between pregnancy and 8 weeks postnatal was 3.0% (N = 27), and 4.6% (N = 42) between 8 weeks postnatal and 1 year postnatal. The overall rate of any postnatal depression onset (at any point postnatally) with no depression in pregnancy was 6.4% (N = 58).

The proportion of the sample with onset of anxiety symptoms between pregnancy and 8 weeks postnatal was 5.0% (N = 45) and 4.6% (N = 42) between 8 weeks postnatal and 1 year postnatal. The overall rate of any onset of postnatal anxiety symptoms with no anxiety in pregnancy was 8.7% (N = 79). The proportion of the sample with onset of somatic symptoms between pregnancy and 8 weeks postnatal was 2.0% (N = 18), and 7.3% (N = 66) between 8 weeks postnatal and 1 year postnatal. The overall rate of any onset of postnatal somatic symptoms with no somatising in pregnancy was 5.3% (N = 48).

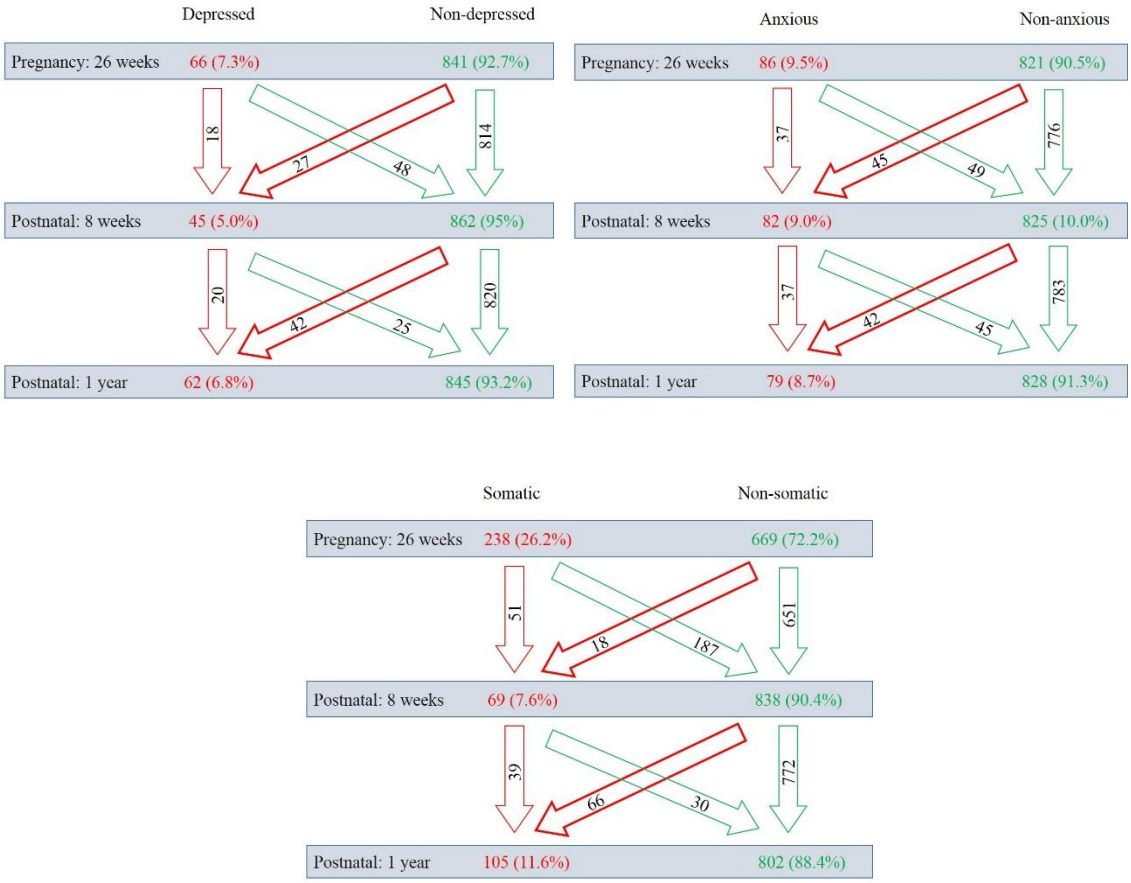

Figure 3. Prevalence and changes in "caseness" of depression, anxiety and somatic symptoms in the perinatal period

Note. Here, "caseness" refers to symptoms above the recommended clinical cut-off on self-report screening tools (depression; PHQ-8; anxiety; GAD-7; somatic; PHQ-15). The arrows illustrate the four possible outcomes between one time-point and the next during the course of the study (stay symptomatic, become unsymptomatic, become symptomatic, stay unsymptomatic). For simplification, the arrows only reflect changes in "caseness" between one time-point and the next immediate time-point and do not illustrate all the possible changes in "caseness" over the three time-points (8 possible outcomes).

Life events as a predictor of depression symptoms in the perinatal period

Cross-sectional associations.

The presence and type of life events experienced in the previous six months was explored as a predictor of depression symptoms cross-sectionally at all three time-points (26 weeks pregnancy, 8 weeks postnatal, 1 year postnatal). Three logistic models compared life events as a predictor of depression:

i) unadjusted univariable model;

ii) a model adjusted for demographic variables (age and deprivation);

iii) a final model adjusted for demographic variables and comorbid anxiety and somatic symptoms.

These models are referred to as model 1, 2 and 3 respectively in the text.

Time 1: 26 weeks pregnancy.

Presence of life events at 26 weeks pregnancy.

From Table 5, it can be seen that Model 1 indicates that having one or more life events (N = 185) was associated with an 80% increase in the odds of having depressive symptoms during pregnancy (OR 1.8, CI 1.03-3.09, $p < .05$) compared with having no life events. Model 2 shows that this relationship was attenuated and became not significant when adjusted for demographics (OR 1.7, CI 0.95-2.91, $p = 0.08$), although the size of the effect and CI width only marginally changed. Adjusting for demographic factors showed that women over the age of 40 had three times the odds of experiencing depression symptoms than women in their thirties. In the fully adjusted model (Model 3), the main effect for life events and depression was no longer significant (OR 1.3, CI 0.67-2.69, $p = 0.41$); however, the presence of comorbid anxiety and somatic symptoms was associated with 14 and 10 times greater odds of having depression symptoms, respectively. However, the wide CI around the OR for anxiety and somatic symptoms indicates imprecise estimation of the effect size for these factors. Nevertheless, these data indicate that, cross-sectionally, comorbid anxiety and somatic symptoms have a much stronger association with depression symptoms than the presence of life events in general.

A test of the fully adjusted model against a constant only model indicated that Model 3 was significantly better at predicting depression symptoms at 26 weeks than the constant-only model (Model X^2 (7) = 176.24, $p < .001$). The Hosmer-Lemeshow goodness-of-fit test indicated that the model fit the data relatively well ($p = 0.09$).

Table 5. Multivariable logistic regression model for life events and depression symptoms at 26 weeks pregnancy (depressed; *N* = 66; not depressed; *N* = 841)

	Unadjusted (Model 1)			Demographics (Model 2)			Clinical comorbidity (Model 3)		
Variable	OR	95% CI	*p* value	OR	95% CI	*p* value	OR	95% CI	*p* value
Life events									
0	-			-			-		
≥1	1.8	1.03, 3.09	0.040	1.7	0.95, 2.91	0.077	1.3	0.67, 2.68	0.414
Age (years)									
<20				2.6	0.53, 13.21	0.237	0.9	0.11, 6.98	0.901
21-30				1.2	0.68, 2.05	0.550	1.0	0.50, 1.93	0.960
31-40				-			-		
41-50				3.6	1.37, 9.52	0.009	2.8	0.73, 10.50	0.132
Deprivation				1.0	0.86, 1.07	0.453	1.0	0.90, 1.16	0.725
Anxiety									
No							-		
Yes							14.0	7.42, 26.55	0.000
Somatising									
No							-		
Yes							10.5	5.14, 21.61	0.000

Types of life events at 26 weeks pregnancy.

Each of the 12 life events were investigated in a series of univariable models with depression at 26 weeks pregnancy as the outcome (Table 6). Significant predictors ($p < .05$) were taken forward into the multivariable model. Model 1 shows that a breakdown in a romantic relationship ($N = 6$) increased the odds of having depression symptoms by six times when compared with women who did not report this event (OR 6.5, CI 1.18-36.38, $p < .05$). This relationship was attenuated and became non-significant in Model 2 when adjusted for demographics (OR 5.7, CI 0.98-33.09, $p = 0.053$). Additionally, this second model showed that women over 40 years old were associated with a fourfold increased risk of having depression. In Model 3, comorbid anxiety and somatic symptoms were associated with increasing the odds of depression by 14 and 10 times respectively. However, the wide CI indicate that the estimates are not precise. The effect of relationship breakdown remained non-significant in Model 3, although it was at the cut-off for statistical significance (OR 10.3, CI 1.00-106.00, $p = 0.05$). A test of the fully adjusted model against a constant-only model indicated that Model 3 was significantly better at predicting the outcome than the constant-only model (Model X^2 (7) = 178.72, $p < .001$). The Hosmer-Lemeshow goodness-of-fit test indicated that the model was relatively well-fitted ($p = 0.17$).

Table 6. Multivariable logistic regression model for types of life events and depression symptoms at 26 weeks pregnancy (depressed; *N* = 66; not depressed; *N* = 841)

	Unadjusted (Model 1)				Demographics (Model 2)				Clinical comorbidity (Model 3)			
		95% CI				95% CI				95% CI		
Variable	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value
Relationship breakdown												
No	-				-				-			
Yes	6.5	1.18	36.38	0.032	5.7	0.98	33.09	0.053	10.3	1.00	105.99	0.050
Age (years)												
<20					3.0	0.61	14.84	0.175	0.92	0.11	7.51	0.936
21-30					1.1	0.66	1.99	0.621	0.96	0.49	1.90	0.910
31-40					-				-			
41-50					3.6	1.36	9.61	0.01	2.8	0.75	10.43	0.125
Deprivation					1.0	0.86	1.06	0.389	1.01	0.89	1.15	0.830
Anxiety												
No					-				-			
Yes									14.4	7.57	27.34	0.000
Somatising												
No					-				-			
Yes									10.8	5.25	22.19	0.000

Time 2: 8 weeks postnatal.

Presence of life events at 8 weeks postnatal.

From Table 7, it can be seen that Model 1 indicates that that having one or more life events (*N* = 191) was associated with a twofold increase in the odds of having depression symptoms at 8 weeks postnatal (OR 2.4, CI 1.28-4.49, $p < .01$) than having no life events. Model 2 shows that this relationship persisted after adjusting for demographics (OR 2.3, CI 1.22-4.32, $p < .05$). This relationship became non-significant when adjusted for comorbid anxiety and somatic symptoms in Model 3 which were both significant predictors of postnatal depression symptoms (OR 1.7, CI 0.78-3.83, $p = 0.18$). Model 3 also shows that comorbid anxiety symptoms were associated with 30 times the odds of having postnatal depression symptoms and comorbid somatic symptoms were associated with six times the odds. However, the wide CI may suggest that these are not precise estimates.

A test of the fully adjusted model against a constant-only model indicated that Model 3 was significantly better at predicting the outcome than the constant-only model (Model X^2 (7) = 152.89, $p < .001$). However, the Hosmer-Lemeshow goodness-of-fit test indicated that the model was not a good fit of the data ($p = 0.01$), meaning that the

observed model was significantly different to the expected model. In addition, four observations were identified from analysis of the residuals which either had standardised residuals values larger than six, deviance residuals larger than two or had a large effect on the chi-square fit statistic relative to other observations. Notably, these four observations had depression and somatic symptoms but without anxiety symptoms which was a minority proportion of the sample (see Table 3), and either experienced zero or one life event.

These four observations were removed from the sample to see whether the model fitted the remaining data better. The multivariable model was run again and the new fully adjusted stringent model (Model 3.1) showed similar non-significant associations between having one or more life events and depression at 8 weeks postnatal (OR 1.4, CI 0.61-3.40, $p = 0.40$) to the original analyses (Model 3, OR 1.7, CI 0.78-3.83, $p = 0.18$). Moreover, the CI for both the original and stringent model overlapped substantially indicating that the variance of the data has not been changed by removing these residuals (see Appendix G for full results of stringent multivariable Model 3.1 in Table 6.1). The Hosmer-Lemeshow goodness-of-fit test indicated that the new stringent model (Model 3.1) was relatively well-fitted ($p = 0.63$). Given that the four observations that were removed represented valid data from this sample and that they make little difference to the clinical interpretation of the results, the original analysis containing all of the data was preferred. Nevertheless, data from the original fully adjusted model (Model 3) should be interpreted with some caution.

Table 7. Multivariable logistic regression model for life events and depression symptoms at 8 weeks postnatal (depressed; *N* = 45; not depressed; *N* = 862)

	Unadjusted (Model 1)				Demographics (Model 2)				Clinical comorbidity (Model 3)			
		95% CI				95% CI				95% CI		
Variable	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value
Life events												
0	-				-				-			
≥1	2.4	1.28	4.49	0.006	2.3	1.22	4.32	0.01	1.7	0.78	3.83	0.177
Age (years)												
<20					4.8	0.93	25.17	0.061	1.2	0.12	10.85	0.897
21-30					1.7	0.89	3.25	0.108	2.3	1.02	5.22	0.045
31-40					-				-			
41-50					2.8	0.78	10.22	0.114	2.3	0.48	11.07	0.300
Deprivation					1.0	0.86	1.11	0.707	1.0	0.87	1.22	0.742
Anxiety												
No					-				-			
Yes									31.5	14.17	69.88	0.00
Somatising												
No					-				-			
Yes									5.9	2.52	14.00	0.00

Types of life events at 8 weeks postnatal.

Each life event was investigated in univariable models with depression at 8 weeks postnatal as the outcome and those that were significant predictors ($p < .05$) were taken forward into the multivariable model (Table 8). Serious financial problems (N = 16) was significantly associated with depression in the univariable model (Model 1) (OR 4.7, CI 1.28-17.0, $p < .05$) and this relationship persisted when adjusted for demographics (Model 2) with little change to the estimate (OR 4.2, CI 1.09-16.0, $p < .05$). Model 2 shows that having serious financial problems increased the odds of having depression symptoms by four times when compared with not having financial problems. However, this relationship was attenuated and became non-significant with comorbid anxiety and somatic symptoms in the fully adjusted model (Model 3) (Table 7, OR 1.7, 0.28-9.7, $p = 0.058$). Comorbid anxiety and somatic symptoms were both independently associated with significant increases in the odds of having depression (anxiety OR 32.1, 14.41-71.46, $p < .01$, somatic OR 6.0, CI 2.51-14.47, $p < .01$). Nevertheless, the wide CI indicate that the estimates of the effect are not precise.

A test of the fully adjusted model against a constant-only model indicated that Model 3 was significantly better at predicting the outcome than the constant-only model (Model X^2 (7) = 151.42, p < .001). However, the Hosmer-Lemeshow goodness-of-fit test indicated that the model was not a good fit ($p = 0.000$), meaning that the observed

model was significantly different to the expected model. In addition, 17 observations were identified from analysis of the residuals which had standardised residuals values larger than three, deviance residuals larger than two or had a large effect on the chi-square fit statistic relative to other observations. Notably, these 17 observations were a mixture of cases with comorbid depression and somatic symptoms but without anxiety symptoms, or did not have any depression, anxiety, somatic symptoms or life events at 8 weeks postnatal. The Hosmer-Lemeshow goodness-of-fit test showed that removal of these observations did not result in a new stringent model (Model 3.1) that fitted the data better (p = 0.000) (see Appendix H for results of the stringent Model 3.1 in Table 7.1). Therefore, the original analyses containing all of the data was preferred (Model 3). Nevertheless, data from the original fully adjusted model (Model 3) should be interpreted with caution.

Table 8. Multivariable logistic regression model for types of life events and depression symptoms at 8 weeks postnatal (depressed; N = 45; not depressed; N = 862)

	Unadjusted (Model 1)				Demographics (Model 2)				Clinical comorbidity (Model 3)			
		95% CI				95% CI				95% CI		
Variable	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value
Financial crisis												
No	-				-				-			
Yes	4.7	1.28	17.00	0.020	4.2	1.09	16.02	0.037	1.7	0.28	9.70	0.577
Age (years)												
<20					4.7	0.89	25.01	0.069	1.0	0.10	10.46	0.980
21-30					1.8	0.92	3.34	0.089	2.2	1.00	5.07	0.051
31-40					-				-			
41-50					2.7	0.74	9.88	0.134	2.2	0.44	10.40	0.341
Deprivation					1.0	0.85	1.10	0.613	1.0	0.87	1.21	0.789
Anxiety												
No									-			
Yes									32.1	14.41	71.46	0.000
Somatising												
No									-			
Yes									6.0	2.51	14.47	0.000

Time 3: 1 year postnatal.

Presence of life events of 1 year postnatal.

Table 9 shows that having one or more life events (N = 211) was significantly associated with a two-fold increase in the odds of having depression at 1 year postnatal in the unadjusted model (Model 1) (OR 2.2, CI 1.30-3.80, p < .01), and this relationship

persisted when adjusted for demographics (Model 2), with a similar estimate and CI (Table 8, OR 2.2, CI 1.28-3.77, $p < .01$). In the fully adjusted model (Model 3), this relationship was attenuated and became non-significant with comorbid anxiety and somatic symptoms (OR 0.85, CI 0.41-1.84, $p = 0.71$). Model 3 shows that comorbid anxiety and somatic symptoms, and being under the age of 20 years old, were significantly associated with large increases in the odds of having depression (anxiety OR 36.8, CI 17.59-76.82, $p < .01$; somatic OR 4.6, CI 2.23-9.81, $p < .01$; age < 20 OR 8.2, CI 1.52-43.95, $p < .05$). However the large CI indicate that these effects are not precisely estimated. A test of the fully adjusted model against a constant only-model indicated that Model 3 was significantly better at predicting the outcome than the constant-only model (Model X^2 (7) = 195.97, $p < .001$). The Hosmer-Lemeshow goodness-of-fit test indicated that the model was relatively well-fitted ($p = 0.46$).

Table 9. Multivariable logistic regression model for life events and depression symptoms at 1 year postnatal (depressed; $N = 62$; not depressed; $N = 845$)

	Unadjusted (Model 1)				Demographics (Model 2)				Clinical comorbidity (Model 3)			
		95% CI				95% CI				95% CI		
Variable	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value
Life events												
0	-				-				-			
≥1	2.2	1.30	3.80	0.004	2.2	1.28	3.76	0.004	0.9	0.41	1.84	0.705
Age (years)												
<20					2.6	0.53	12.72	0.241	8.2	1.52	43.95	0.014
21-30					1.3	0.74	2.23	0.383	1.1	0.51	2.22	0.876
31-40					-				-			
41-50					1.9	0.54	6.68	0.317	1.0	0.16	5.83	0.973
Deprivation					0.9	0.80	0.98	0.020	0.9	0.78	1.02	0.084
Anxiety												
No					-				-			
Yes									36.8	17.59	76.82	0.000
Somatising												
No					-				-			
Yes									4.7	2.23	9.81	0.000

Types of life events at 1 year postnatal.

Each life event was investigated in univariable models with depression at 1 year postnatal as the outcome and those that were significant predictors ($p < .05$) were taken forward into the multivariable model (Table 10). Having a breakdown in romantic relationship ($N = 9$), becoming unemployed ($N = 31$) and serious financial problems ($N = 21$) were significantly associated with depression in univariable models and so they were taken forward into multivariable models and entered simultaneously. When

entered simultaneously as a set of predictors, relationship breakdown and serious financial problems remained significant independent predictors of each other, but unemployment did not (Model 1). Women who had a relationship breakdown had nearly seven times the odds of experiencing depression (OR 6.6, CI 1.54-28.26, $p < .05$) and women reporting serious financial problems had four times the odds of experiencing depression (OR 4.4. CI 1.56-12.36, $p < .01$) than women who did not report these events (Model 1). These relationships persisted when adjusted for demographics (Model 2), though the odds of experiencing depression after having serious financial problems was slightly reduced. However, the wide CI indicate that these are not precise estimates.

Table 10 shows that the relationship between these life events and depression was attenuated and became non-significant when adjusted for comorbid anxiety and somatising symptoms (Model 3) (relationship breakdown OR 4.7, CI 0.50-44.12, $p = 0.17$; serious financial problems OR 0.63, CI 0.16-2.47, $p = 0.51$). Having comorbid anxiety and somatic symptoms were both independently associated with increased odds of having depression symptoms: comorbid anxiety increased the odds by 36 times (OR 36.1, CI 17.39-74.85, $p < .01$) and comorbid somatic symptoms increased the odds by five times (OR 5.0, CI 2.30-10.75, $p < .01$). Additionally, women under 20 years old had over eight times the odds of depression than women in their thirties in the fully adjusted model (Model 3) (OR 8.4, CI 1.56-45.56, $p < .05$). A test of the fully adjusted model against a constant-only model indicated that Model 3 was significantly better at predicting the outcome than the constant-only model (Model $X^2 (7) = 198.31$, $p < .001$). The Hosmer-Lemeshow goodness-of-fit test indicated that the model was relatively well-fitted ($p = 0.71$).

Table 10. Multivariable logistic regression model for types of life events and depression symptoms at 1 year postnatal (depressed; *N* = 62; not depressed; *N* = 845)

	Unadjusted (Model 1)				Demographics (Model 2)				Clinical comorbidity (Model 3)			
	95% CI				95% CI				95% CI			
Variable	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value
Relationship breakdown												
No	-				-				-			
Yes	6.6	1.54	28.26	0.011	7.9	1.85	33.51	0.005	4.7	0.50	44.12	0.174
Unemployment												
No	-				-				-			
Yes	2.2	0.75	6.23	0.153	2.1	0.70	6.16	0.187	0.7	0.17	3.16	0.674
Financial crisis												
No	-				-				-			
Yes	4.4	1.56	12.36	0.005	3.8	1.35	10.91	0.012	0.6	0.16	2.47	0.509
Age (years)												
<20					2.8	0.55	13.86	0.217	8.4	1.56	45.56	0.013
21-30					1.3	0.76	2.32	0.325	1.1	0.52	2.27	0.832
31-40					-				-			
41-50					1.8	0.49	6.38	0.389	1.2	0.20	7.62	0.816
Deprivation					0.9	0.80	0.99	0.029	0.9	0.76	1.01	0.062
Anxiety												
No					-				-			
Yes									36.1	17.39	74.85	0.000
Somatising												
No					-				-			
Yes									5.0	2.30	10.75	0.000

Summary of cross-sectional analyses.

Having one or more life events significantly predicted depression symptoms (PHQ-8 ≥10) during the first year after birth (Tables 7 and 9) but not during pregnancy (Table 5), after adjusting for age and deprivation levels. Having one or more life events in the postnatal period was associated with nearly double the odds of having postnatal depression symptoms, although the CI indicated it could increase the odds by up to four times (Tables 6 and 8).

The relationship between life events and concurrent depression was attenuated and became non-significant when adjusted for comorbid anxiety and somatic symptoms at all time-points during the perinatal period. Anxiety and somatic symptoms were consistently associated with much larger increases in the odds of having depression than life events alone and, thus, appear to be stronger predictors of depression than life events when examined cross-sectionally.

Regarding specific types of life events, romantic relationship breakdown and serious financial problems were associated with larger increases in the odds of having depression across the perinatal period than the presence of life events in general, although small sample sizes meant the effect size could not be precisely estimated. Relationship breakdown conferred greater risk of depression during early to mid-pregnancy, whilst serious financial problems were associated with greater risks during mid-pregnancy to the early postnatal period, and both relationship breakdown and serious financial problems occurring during the second half of the first postnatal year were associated with depression at 1 year postnatal.

Prospective associations

The cross-sectional models described above demonstrate that life events are important predictors of depression at static time-points throughout the perinatal period. This chapter further explores whether life events during pregnancy are associated with depression during the postnatal period, whilst adjusting for antenatal depression, anxiety and somatic symptoms. Additionally, this chapter examines the relationship between depression, anxiety and somatic symptoms across time, given that anxiety and somatic symptoms were significant predictors of depression cross-sectionally.

As described in the Method chapter (see *Outcome variable, Prospective analyses*) an initial set of exploratory logistic regression models were used to determine the optimal method for constructing postnatal depression outcome. This indicated that the prevalence of depression at 8 weeks postnatal (5.0%) and 1 year postnatal (6.8%) would result in under-powered analyses if depression outcome was modelled separately at each time-point. Therefore, depression prevalence at 8 weeks and 1 year postnatal was combined (9.6%) to enable a sufficiently powered prospective analysis. Additionally, the postnatal depression onset variable (defined as all new cases of depression during the postnatal period in those free from depression during pregnancy) was not an effective way of modelling the relationship between life events and depression, given that the number of cases of onset of postnatal depression was relatively low (N = 58, 6.4%) and the analyses would be under-powered. See Appendix I for results of the sensitivity analysis showing the results of the exploratory model examining life events as predictor of postnatal depression that has its onset postnatally. On the other hand, the overall prevalence of postnatal depression was higher (N = 87, 9.6%) and provided sufficient statistical power to model the effect of life events on depression. Therefore, the outcome variable was modelled dichotomously as the

presence or absence of depression during the postnatal period. Some cases of postnatal depression would have had their onset in the antenatal period, therefore, all prospective models were adjusted for the presence of antenatal depression in order to control for the increased odds of having postnatal depression following antenatal depression.

Similarly, it was not possible to investigate how life events might be differentially associated with postnatal depression at 8 weeks postnatal (N = 45) compared with 1 year postnatal (N = 62) due to small numbers of women with postnatal depression symptoms, so they were combined in the analyses to represent postnatal depression at any point in the year after birth.

Prospective associations between life events occurring during pregnancy through to the early postnatal period and postnatal depression were examined, with one model including life events during early to mid-pregnancy and a second, life events during mid-pregnancy to the early postnatal period (see *Method* chapter).

For each of the two prospective periods, four logistic models compared life events as a predictor of postnatal depression (8 weeks and 1 year postnatal combined):

i) unadjusted
ii) adjusted for antenatal depression
iii) adjusted for antenatal depression and demographics (age and deprivation);
iv) adjusted for antenatal depression, demographics and antenatal anxiety and somatic symptoms.

These models are referred to as model 1, 2, 3 and 4 respectively in the text.

Life events in early to mid- pregnancy.

Presence of life events in early to mid-pregnancy.

Having one or more life events during early to mid-pregnancy was not significantly associated with postnatal depression in the univariable analysis compared with having no life events (Model 1) (OR 1.6, CI 0.95-2.57, p = 0.08). Therefore, life events were not analysed further in multivariable regression models. Consistent with the non-significant association found in regression analyses, a test of the univariable model against a constant-only model indicated that including life events as the only predictor was not significantly better at predicting the outcome (Model X^2 (1) = 2.86, p = 0.09). The Hosmer-Lemeshow goodness of fit test could not be conducted on the univariable

model (Model 1) because it only contained one dichotomous predictor (none versus one or more life events).

Types of life events in early to mid-pregnancy.

Each life event was investigated individually in univariable models with postnatal depression as the outcome and those that were significant predictors ($p < .05$) were taken forward into the multivariable model (Table 11). In univariable analysis, having a serious problem with a close friend, relative or neighbour ($N = 27$) during early to mid-pregnancy was significantly associated with an increase in the odds of postnatal depression by 3.5 times (Model 1) (OR 3.5, CI 1.44-8.53, $p < .01$) and so was taken forward into the multivariable model. The significant relationship persisted after adjusting for antenatal depression (Model 2), demographics (Model 3) and antenatal anxiety and somatic symptoms (Model 4), although the OR and CI were reduced slightly (OR 2.8, CI 1.01 – 7.91, $p < .05$). The increase in risk of postnatal depression conferred by having problems with a close friend or relative was similar to that conferred by antenatal depression symptoms (OR 2.5, CI 1.22-5.19, $p < .05$), and antenatal somatic symptoms (OR 2.4, CI 1.37-4.08, $p < .01$). On the other hand, antenatal anxiety symptoms increased the odds of postnatal depression by approximately six times (OR 6.1, CI 3.26-11.59, $p < .01$). A test of the fully adjusted model against a constant-only model indicated that Model 4 was significantly better at predicting the outcome than the constant-only model (Model X^2 (8) = 117.19, $p < .05$). The Hosmer-Lemeshow goodness-of-fit test indicated that the model was relatively well-fitted ($p = 0.27$).

Table 11. Multivariable logistic regression model for types of life events during early to mid-pregnancy and postnatal depression symptoms (depressed; *N* = 87; not depressed; *N* = 82)

	Unadjusted (Model 1)				Antenatal Depression (Model 2)				Demographics (Model 3)				Antenatal Comorbidity (Model 4)			
		95% CI				95% CI				95% CI				95% CI		
Variable	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value
Social/friendship problem																
No	-				-				-				-			
Yes	3.5	1.44	8.53	0.006	3.2	1.19	8.45	0.021	2.8	1.01	7.79	0.049	2.8	1.01	7.91	0.048
Antenatal Depression																
No					-				-				-			
Yes					10.4	5.95	18.18	0.000	10.2	5.79	18.08	0.000	2.5	1.22	5.19	0.013
Age (years)																
<20									3.6	0.82	15.45	0.089	2.6	0.54	12.32	0.237
21-30									1.1	0.69	1.90	0.590	1.1	0.63	1.83	0.799
31-40									-				-			
41-50									1.1	0.33	3.70	0.864	0.8	0.22	2.82	0.704
Deprivation									0.9	0.84	1.01	0.090	0.9	0.85	1.04	0.215
Antenatal Anxiety																
No									-				-			
Yes													6.1	3.26	11.59	0.000
Antenatal Somatising																
No									-				-			
Yes													2.4	1.37	4.08	0.002

Life events in mid-pregnancy to early postnatal period.

Presence of life events in mid-pregnancy to early postnatal period.

Table 12 shows that having one or more life events during mid-pregnancy through to the early postnatal period (N = 191) was significantly associated with postnatal depression in the unadjusted model (Model 1) (OR 1.9, CI 1.18-3.10, $p < .01$). The association persisted after adjusting for antenatal depression (Model 2) and demographics (Model 3). The odds of having postnatal depression symptoms were increased by 80% in women who experienced one or more life events, compared with women did not have any life events (OR 1.8, CI 1.10-3.12, $p <.05$). However, this effect was attenuated to below significance in the fully adjusted model (Model 4) (OR 1.7, CI 0.99-2.97, $p = 0.05$) after adjusting for antenatal anxiety and somatic symptoms which were significant independent predictors of depression. Antenatal depression and somatic symptoms similarly increased the odds of postnatal depression by approximately 2.5 times whilst antenatal anxiety symptoms increased the odds by nearly six times. A test of the fully adjusted model against a constant-only model indicated that Model 4 was significantly better at predicting the outcome than the constant-only model (Model X^2 (7) = 12.61, $p < .05$). The Hosmer-Lemeshow goodness-of-fit test indicated that the model was relatively well-fitted ($p = 0.16$).

Table 12. Multivariable logistic regression model for the presence of life events during mid-pregnancy to the early postnatal period and postnatal depression symptoms (depressed; *N* = 87; not depressed; *N* = 820)

	Unadjusted (Model 1)				Antenatal Depression (Model 2)				Demographics (Model 3)				Antenatal Comorbidity (Model 4)			
		95% CI				95% CI				95% CI				95% CI		
Variable	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value
Life events																
0	-				-				-				-			
≥1	1.9	1.18	3.10	0.008	2.0	1.17	3.26	0.011	1.9	1.10	3.12	0.020	1.7	0.99	2.97	0.054
Antenatal Depression																
No					-				-				-			
Yes					10.7	6.10	18.70	0.000	10.5	5.93	18.63	0.000	2.6	1.23	5.34	0.012
Age (years)																
<20									4.3	1.04	17.91	0.044	3.2	0.66	15.22	0.150
21-30									1.1	0.69	1.89	0.611	1.0	0.61	1.79	0.861
31-40									-				-			
41-50									1.0	0.30	3.49	0.963	0.7	0.20	2.74	0.657
Deprivation									0.9	0.85	1.02	0.145	0.9	0.85	1.04	0.266
Antenatal Anxiety																
No									-				-			
Yes													5.9	3.13	11.20	0.000
Antenatal Somatising																
No									-				-			
Yes													2.4	1.39	4.15	0.002

Types of life events in mid-pregnancy to early postnatal period.

Each life event during mid-pregnancy was investigated individually in univariable models with postnatal depression as the outcome. Significant predictors ($p < .05$) were taken forward into the multivariable model presented in Table 13. Having a serious problem with a close friend, relative or neighbour ($N = 27$) and having serious financial problems ($N = 16$) were entered simultaneously into the multivariable models. When entered simultaneously, Model 1 shows that the effect of financial problems became non-significant when controlling for having serious problems with a close friend, relative or neighbour which was an independent predictor of postnatal depression; increasing the odds of postnatal depression by three times (OR 3.1, CI 1.27-7.84, $p < .05$). This effect persisted after adjusting for antenatal depression (Model 2), demographics (Model 3), and antenatal anxiety and somatic symptoms (Model 4), with a slightly larger OR and CI (OR 3.7, CI 1.35-10.0, $p < .05$). However, the wide CI indicate that the effect is not estimated precisely.

Nevertheless, having serious problems with a close friend, relative or neighbour during mid-pregnancy to the early postnatal period resulted in larger increases in the odds of having postnatal depression than antenatal depression or somatic symptoms which themselves increased the risk by approximately two times. Antenatal anxiety symptoms had the largest associations with postnatal depression, increasing the odds by nearly six times.

A test of the fully adjusted model against a constant-only model indicated that Model 4 was significantly better at predicting the outcome than the constant-only model (Model X^2 (9) = 120.24, $p < .01$). However, the Hosmer-Lemeshow goodness-of-fit test indicated that the model was not a good fit ($p = 0.03$). In addition, one observation was identified from analysis of the residuals which had standardised residuals values larger than six, the largest deviance residual (>2) and had a large effect on the chi-square fit statistic relative to other observations. This case reported no depression, anxiety or somatic symptoms, or life events at baseline (26 weeks pregnancy) but experienced depression and anxiety symptoms at 8 weeks postnatal along with one life event. The multivariable model was run again with this single observation excluded and the new fully adjusted stringent model (Model 4.1) showed similar but marginally larger estimates of the effect of having serious problems with a close friend, relative or neighbour during mid-pregnancy to the early postnatal period on postnatal depression (Model 4.1, OR 3.9, CI 1.43-10.65, $p < .01$) to the original analyses (Model 4, OR 3.7, CI 1.35-10.0, $p < .05$) (see Appendix J for full results of the stringent multivariable

Model 4.1 in Table 13.1). The Hosmer-Lemeshow goodness-of-fit test indicated that the new stringent model was relatively well-fitted ($p = 0.09$). Given that the single observation removed represented valid data from this sample and that it made little difference to the clinical interpretation of the results, the original analyses containing all of the data is preferred. Nevertheless, data from the original fully adjusted model (Model 4) should be interpreted with some caution.

Table 13. Multivariable logistic regression model for types of life events during mid-pregnancy to the early postnatal period and postnatal depression symptoms (depressed; *N* = 87; not depressed; *N* = 820)

	Unadjusted (Model 1)				Antenatal Depression (Model 2)				Demographics (Model 3)				Antenatal Comorbidity (Model 4)			
	95% CI				95% CI				95% CI				95% CI			
Variable	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value
Social/friendship problem																
No	-				-				-				-			
Yes	3.1	1.27	7.84	0.014	3.6	1.37	9.46	0.009	3.4	1.25	9.00	0.016	3.7	1.35	10.00	0.011
Financial crisis																
No	-				-				-				-			
Yes	2.6	0.79	8.68	0.114	3.1	0.87	10.67	0.081	2.8	0.80	10.01	0.105	1.8	0.45	6.84	0.419
Antenatal Depression																
No					-				-				-			
Yes					11.1	6.33	19.47	0.00	10.9	6.16	19.40	0.00	2.7	1.31	5.67	0.008
Age (years)																
<20									3.9	0.96	16.26	0.057	3.1	0.66	14.62	0.153
21-30									1.1	0.68	1.89	0.626	1.0	0.61	1.79	0.874
31-40																
41-50									1.0	0.29	3.23	0.955	0.7	0.20	2.58	0.616
Deprivation									0.9	0.85	1.03	0.153	0.9	0.86	1.05	0.276
Antenatal Anxiety																
No									-				-			
Yes													6.0	3.16	11.34	0.000
Antenatal Somatising																
No									-				-			
Yes													2.4	1.36	4.07	0.002

Summary of prospective models.

Similarly to the cross-sectional models of life events and depression, one or more life events occurring during the early to mid-pregnancy or mid-pregnancy to early postnatal period did not consistently predict postnatal depression (at 8 weeks or 1 year postnatal) across the prospective models investigated. Specifically, modelling life events as a dichotomous (none versus one or more) predictor was either not significantly associated with postnatal depression in the unadjusted analyses or did not remain an independent predictor in the presence of antenatal anxiety and somatic symptoms in the adjusted models.

On the other hand, certain types of life events were more consistent predictors of depression postnatally. Having serious problems with a close friend, relative or neighbour during pregnancy or in the early postnatal period significantly increased the odds of having postnatal depression by approximately threefold, after adjusting for demographics and antenatal depression, anxiety and somatic symptoms (Tables 10 and 12).

Compared to the cross-sectional associations between comorbid anxiety and somatic symptoms and depression, prospective analysis of these factors suggest that antenatal comorbidity had more modest associations with postnatal depression (at 8 weeks or 1 year postnatal). The CI also indicated that these were relatively more precise estimates of effect (Tables 11, 12 and 13) than estimates in the cross-sectional analyses (Tables 5-10). Similar to the cross-sectional models, anxiety was a strong predictor for depression in the prospective analyses, with antenatal anxiety having the largest association with postnatal depression in the multivariable model, even more so than antenatal depression. On the other hand, antenatal depression and antenatal somatic symptoms had similar associations with postnatal depression, both of which were smaller than the effect of a woman having serious problems with a close friend, relative or neighbour in the early to mid-pregnancy or mid-pregnancy to early postnatal period.

Checking the model assumptions

Logistic regression assumes that the independent variables are linearly related to the log of the outcome variable and that there is little to no multicollinearity between independent (predictor) variables (see *Method* chapter). These assumptions were checked for every model although multivariable models with large samples are sufficiently robust to handle departures from assumptions (Katz, 2011). The linearity of the logit was tested by substituting continuous independent variables for a logarithmic

transformation of itself into the model and assessing for improvement in the model fit and size of the estimated effect for that variable (Katz, 2011). There was no evidence of multicollinearity between the independent variables in any of the models as tolerance values were greater than 0.1 ad VIF values were less than 10.

The residuals were also examined in every model to detect evidence of excessive bias, although in large data sets it is less likely that the results will be influenced by one or two extreme observations (Katz, 2011). Moreover, residuals that are at the extreme ends are more likely in models where there are strong dichotomous predictors (Katz, 2006) such as anxiety and somatic symptoms in this study. Nevertheless, in the models which were relatively well-fitted (as indicated by the Hosmer-Lemeshow goodness-of-fit tests), less than 5% of standardised residuals had values greater than two. In the models which were not well-fitted, the most influential observations were identified by examination of the residuals and excluded from the analysis. The Hosmer-Lemeshow goodness-of-fit test indicated that the new stringent multivariable models were well-fitted, apart from one model (Model 3.1, cross-sectional analyses at 8 weeks postnatal) (see Appendix G). On the whole, the new stringent models showed little change in the size of the effect of life events on depression and the precision of the estimate to the original models, as would be expected in models with large sample sizes (Katz, 2011). This suggests that the residuals were of little cause of concern in the interpretation of the model.

Post-hoc sample size calculation

A post-hoc sample size calculation was calculated for each of the cross-sectional and prospective logistic regression models (see *Method* chapter). The sample size calculation was based on the prevalence of perinatal depression at 26 weeks pregnancy (7.3%), 8 weeks postnatal (5.0%) and 1 year postnatal (6.8%), and the number of predictors in the model. For example, at 26 weeks pregnancy, a prevalence of depression at 7.3% with seven predictors in the logistic regression models leads to a conservative sample size estimate of 958 needed to model the association between life events and depression. Sample size estimates for the remaining cross-sectional models were 1400 at 8 weeks postnatal and 1029 at 1 year postnatal. This indicates that the cross-sectional models were slightly under-powered (actual $N = 907$). Based on the prevalence of postnatal depression in the prospective models (9.6%) with eight predictors in the model, a conservative estimate of the sample size needed for the

prospective logistic regression model is 833. This indicates that the prospective models were sufficiently powered to detect an effect (actual $N = 907$).

Discussion

This chapter begins by summarising the general findings of this study in relation to the depression, anxiety and somatic symptoms experienced by the women in this sample across the perinatal period. The main associations between the number and type of life events with perinatal depression across the cross-sectional and prospective analyses are then reviewed and discussed. Finally, this chapter concludes with a discussion of the strengths and limitations of this study, clinical implications and potential areas of future research.

Summary of findings

Depression, anxiety and somatic symptoms in the perinatal period.

Prevalence.

One of the aims of this study was to examine the prevalence of self-reported depression, anxiety and somatic symptoms over the perinatal period in this population cohort. This study found the point prevalence estimates of depression symptoms in this sample across the perinatal period (7.3% during pregnancy, 5.0-6.8% during postnatal period) to be similar to those reported for major depression by recent systematic reviews (Gavin et al., 2005, Woody et al., 2017). Notably, the prevalence at 26 weeks pregnancy in this sample (7.3%) was similar to that obtained in a large pregnant sample in the United States using the same self-report depression measure (6.1%) (Ashley, Harper, Arms-Chavez, & LoBello, 2016). The prevalence of anxiety symptoms were higher than that of depression symptoms in this sample in keeping with the greater prevalence of anxiety disorders over other mood disorders in the general population (Kessler et al., 2005) and perinatal population (Fairbrother et al., 2016; Giardinelli et al., 2012; Reck et al., 2008; Wenzel et al., 2005; Wynter et al., 2013).

The point prevalence estimates of anxiety symptoms across the perinatal period in this study (8.7-9.5%) were within ranges of prevalence estimates reported in the literature (e.g., 4.1-16.0% antenatally, 2.4-18.0% postnatally; Leach, Poyser, & Fairweather-Schmidt, 2017). The prevalence of anxiety was highest during pregnancy and gradually decreased over the postnatal period, in keeping with the findings of other studies (Leach et al., 2017). Estimates of depression and anxiety comorbidity in this study (approximately 5% in the perinatal period) are similar to those previously reported in the literature (Fairbrother et al., 2016; Matthey et al., 2003). Approximately

two-thirds of women with self-reported depression symptoms also reported having comorbid anxiety symptoms across the perinatal period. This is higher than previously reported estimates of the proportion of women with diagnoses of perinatal depression who also have perinatal anxiety disorder diagnoses (as assessed by a structured clinical interview) (e.g., 33.9%; Reck et al., 2008). The higher proportion of comorbidity when assessed by self-report measures may reflect the tendency for screening measures to have higher sensitivity than specificity, that is, screening measures will pick up more 'cases' than structured clinical interviews, which are a more reliable diagnostic procedure (Thombs, Kwakkenbos, Levis, & Benedetti, 2018). Nevertheless, postnatal depression has been shown to be associated with higher levels of anxiety symptomatology than depression at other times in a woman's life (Beck & Indman, 2005).

Finally, the prevalence of somatic symptoms found in this study across the perinatal period (7.6-26.2%) was higher than that of depression (5.0-7.3%) or anxiety symptoms (8.7-9.5%). This study is the first to report on the prevalence of perinatal somatic symptoms as assessed by a validated screening measure of somatic symptom disorders and was broadly within the estimates of somatic symptom disorders in the general population (10-25%; Hilderlink et al., 2013).

This study also confirms the findings of previous studies which have reported that depression and anxiety symptoms tend to decrease after childbirth (Heron et al., 2004; Falah-Hassani et al., 2016). Importantly, the reported prevalence of depression, anxiety and somatic symptoms in this study is likely to be an under-estimate of the perinatal population given that women who were excluded from the analyses because of incomplete data (N = 1455) had significantly higher symptoms of depression, anxiety and somatic symptoms during pregnancy than the women in the complete cases group.

Postnatal onset of depression, anxiety and somatic symptoms.

The incidence of postnatal depression and anxiety symptoms in this study (6.4% and 8.7% respectively) are within the ranges previously reported in the literature (6.5% and 8.8% respectively; Gavin et al., 2005; Wenzel et al., 2005). This study is the first to report on the incidence of postnatal somatic symptoms as assessed by a somatic symptom disorder screening measure and found the incidence to be 5.3% of this sample.

Changes in depression, anxiety and somatic symptoms "caseness".

The present study also confirms previous findings which have shown a reduction in depression symptoms from pregnancy to the early postnatal period (Schmied et al., 2013). Indeed, more women in this study experienced a reduction of depression symptoms (from above to below the clinical cut-off on the PHQ-8) from 26 weeks pregnancy to 8 weeks postnatal (N = 48) than experienced an increase (N = 27). However, this study also showed that a larger proportion of women experienced increases in depression and somatic symptoms (moving from below to above the clinical cut-off) from 8 weeks postnatal to 1 year after childbirth than those who experienced decreases in these symptoms. This is important given that the DSM-V and ICD-10 diagnostic criteria for postnatal depression specify postnatal depression symptoms as developing within four to six weeks after childbirth (APA, 2013; WHO, 1992).

Previous work has identified that there are multiple trajectories of anxiety and depression symptoms across the perinatal period. For example, patterns of symptoms include persistent antenatal to postnatal symptoms, antenatal symptoms only or postnatal symptoms only (Bayrampour et al., 2016). In line with this, this study demonstrated that many individual women moved in and out of clinical "symptom" caseness over time even though the prevalence rates of the disorders stayed relatively stable across the three time points in the perinatal period. Indeed, previous work has shown that depression symptoms can be transient and vary in a matter of weeks during pregnancy and the postnatal period (Matthey & Ross-Hamid, 2012; von Ballestrem, Strauß, & Kächele, 2005).

Life events as predictors of depression.

Prevalence.

The pattern of life events that were most commonly experienced in this sample, namely bereavements, health difficulties in others and serious problems with close friends or relatives mirrors those commonly reported in large population cohort studies that have also used the LTE-Q as a life events measure in studies of men and women in in the Netherlands (N = 2981) (Spinhoven et al., 2010) and in Spain (N = 5378) (Motrico et al., 2013).

The majority of women in this study (approximately 60% across the perinatal period) experienced no life events. Most studies using the LTE-Q have reported slightly higher numbers of life events experienced in the general primary care population. For example, 65% of men and women in a Spanish primary care population (N = 5378) experienced one or more life events over a six-month period (Motrico et al., 2013). However, the study used systematic random sampling across seven provinces in Spain and, therefore, is likely to have a more diverse population than the present study sample. Conversely, approximately 28% of women under 50 years old (N = 441) in a Dutch general population sample reported one or more life events on the LTE-Q in the last year (Rosmalen, Bos, & de Jonge, 2012). Importantly, the complete case sample in this study that was used for analysis reported significantly fewer life events on average than the incomplete sample at 26 weeks pregnancy (0.3% vs 0.5% respectively) and thus may potentially also have experienced a smaller number of life events throughout the perinatal period, overall, than the incomplete sample.

Presence of life events.

Cross-sectional associations.

One of the aims of the study was to explore the cross-sectional associations between the number and type of life events and depression symptoms during the perinatal period whilst controlling for age, deprivation and comorbid anxiety and somatic symptoms.

Having one or more life events during pregnancy was found to be associated with 1.8 times greater odds of having antenatal depression in univariable analyses (OR 1.8). This association became non-significant when controlling for age and deprivation although the estimate was only marginally attenuated (OR 1.7). In this study, both younger age (<20 and 21-30 years old) and older age (>40 years old) were associated with increased odds of depression at various times across the perinatal period. Research suggests that age is an inconsistent predictor of perinatal depression, although young age (teenaged mothers) and older age is often associated with depression in correlational analyses (Biaggi et al., 2016). Older mothers tend to have less support from extended family than younger mothers, and pregnant women may be more vulnerable to life events during pregnancy when social support is limited (Bornstein, Putnick, Suwalsky, & Gini, 2006). Women over 40 years old are also at increased risk of hypertension

during pregnancy and obstetric complications (Dietl, Cupisti, Beckmann, Schwab, & Zollner, 2015).

However, the finding that the presence of life events did not predict antenatal depression after controlling for demographics is in contrast to reviews of the literature that have consistently found significant associations between life events and antenatal depression in both univariable and multivariable analyses (Lancaster et al., 2010). One possible explanation for the lack of association in this study was the low number of life events reported in this sample overall, with less than 5% women experiencing two or more life events in a six-month period across the perinatal period. Indeed, other studies of antenatal depression have found an association between greater, but not lower, numbers of life events. For example, Shakeel et al. (2015) found that only three or more life events during pregnancy was associated with antenatal depression, increasing the odds by five times. In a Swedish sample of 3011 women, two or more life events in the past year were associated with three times the odds of having antenatal depression (Rubertsson et al., 2003).

With regard to postnatal depression, having one or more life events was associated with a greater than two-fold increase in risk of having postnatal depression after adjusting for age and deprivation level (OR 2.3, 8 weeks postnatal; OR 2.2, 1 year postnatal). This supports existing literature that have found significant associations between life events and postnatal depression in cross-sectional analyses (Yim et al., 2015). In addition, this strength of effect is similar to previous literature reporting a cross-sectional association between one or more life events on the LTE-Q and depression in the general population. For example, Motrico et al. (2013) found that one or more life events on the LTE-Q in the preceding six months was associated with 1.7 times the odds of having a clinical diagnosis of major depression. In a sample of older adults in the UK (N = 960), one or more life events on the LTE-Q in the preceding year was associated with an increased odds of having depression by 1.8 times (Donoghue et al., 2016).

However, the number of life events experienced did not have independent effects on antenatal or postnatal depression when accounting for comorbid anxiety and somatic symptoms which both had much stronger associations with perinatal depression. This is not surprising given the high proportion of depressed women in this sample who also reported comorbid anxiety symptoms (60.6% antenatally, 71.0-75.6% postnatally) and somatic symptoms (81.8% antenatally, 51.1-58.1% postnatally). In particular, comorbid anxiety symptoms were associated with much larger increases in

the odds of perinatal depression than comorbid somatic symptoms (OR 14-37, OR 5-11 across the perinatal period respectively). Furthermore, the strength of association between anxiety and depression increased from pregnancy (OR 14.0) to the end of the first year postnatal (OR 36.8), whereas somatic symptoms decreased in their association with depression from pregnancy (OR 10.8) to the end of the first postnatal year (OR 4.7). However, the confidence intervals around the odds ratios were very wide, indicating that the model estimations were imprecise. The different strengths of association may possibly reflect the increasing prevalence of depression and comorbid anxiety, and decreasing prevalence of depression comorbid with somatic symptoms, over time from pregnancy to 1 year postnatal. The greater association of anxiety symptoms with depression in the postnatal period may be associated with the increased stress experienced by mothers trying to meet the demands of a baby and ongoing family life when they are struggling with postnatal depression themselves. Indeed, Leigh and Milgrom (2008) showed that postnatal depression at 12 weeks was predictive of higher parenting stress, which in turn may exacerbate or maintain current depression symptoms.

In addition, it is possible that part of the cross-sectional relationship between life events and depression is explained by increasing anxiety and somatic symptoms although this directionality is unclear from cross-sectional analyses. Life events have been found to be related to onset of anxiety symptoms in the general population (e.g., Kendler et al., 2003), although associations with anxiety are generally smaller than that with depression (Motrico et al., 2013).

Prospective associations.

Prospective associations between life events and postnatal depression were examined in two models of life events: i) life events experienced during early-to-mid pregnancy; and ii) life events experienced during the late pregnancy to early postnatal period. In addition, the effects of antenatal depression, anxiety and somatic symptoms on postnatal depression were controlled for. There was no evidence of association between the presence of life events in early-to-mid pregnancy and postnatal depression (at 8 weeks or 1 year postnatal), even in the univariable analyses. This concurs with many longitudinal studies recently reviewed which similarly found no effect between the number of life events experienced during pregnancy and postnatal depression (Yim et al., 2015). The impact of life events is known to lessen over time (Hillegers et al., 2004) so it is possible that the low number or lesser severity of life events experienced

by most women in this sample during pregnancy were not great enough to predict postnatal depression that could potentially develop nearly two years after the event occurred (the prospective period under consideration in this study spanned conception to 1 year postnatal).

However, in model ii, life events that occurred during the late pregnancy to early postnatal period did significantly increase the odds of postnatal depression symptoms (at 8 weeks or 1 year postnatal) by nearly two-fold after adjusting for age and deprivation (OR 1.9). Similar to the present findings, previous literature has evidenced a stronger association between postnatal depression and postnatal life events than with antenatal life events (Swendsen & Mazure, 2000). This may be due to the fact that life events that are closer in proximity to the development of depression have a stronger aetiological role (Hillegers et al., 2004) as well as a possible greater association between postnatal depression and difficulties in adjusting to the demands of caring for a newborn amidst stressful life events in the postnatal period (Swendsen & Mazure, 2000). In the present study, the relationship between late pregnancy to early postnatal life events and postnatal depression was attenuated to below significance after adjusting for antenatal depression, anxiety and somatic symptoms (OR 1.7, CI 0.99-2.97, $p = 0.054$). Milgrom et al. (2008) reported similar findings in their longitudinal study of 7797 Australian women where major life events in the past year (reported at mid-pregnancy) were predictive of postnatal depression (OR 2.5) but not when controlling for antenatal depression and anxiety. This suggests that life events do not uniquely contribute to the risk of postnatal depression over and above the contribution of psychological distress during pregnancy.

Types of life events.

Cross-sectional associations.

The two types of life events that were cross-sectionally associated with increased risk of depression during the perinatal period were relationship breakdown (OR 2.2-2.3 across the perinatal period) and serious financial problems (OR 3.8, 1 year postnatal). Associations between these specific types of events and perinatal depression were generally bigger than those found for the presence of one or more life events alone as a predictor. However, the confidence intervals for the odds ratios were large, indicating that the effect was imprecisely estimated. Similar patterns have been reported in the general population exploring life events (as assessed by the LTE-Q) and

depression. For example, Motrico et al. (2013) found that specific life events in the previous six months, in particular, relationship breakdown (OR 2.6), serious problems with a close friend or relative (OR 2.5) and serious financial problems (OR 1.9) were the most strongly associated with a diagnosis of depression. In another study examining lifetime prevalence of life events and diagnoses of depression in the general population, Spinhoven et al. (2010) reported the three strongest associations with general depression as being lifetime prevalence of serious financial problems (OR 2.6), relationship breakdown (OR 1.9) and serious problems with a close friend or relative (OR 1.8) in univariable analyses.

The findings from this study also confirm the literature on perinatal depression that has found a greater association between relationship life events (Stone et al., 2015; Wright et al., 2015), financial stress (Liu & Tronick, 2013; Yim et al., 2015) and perinatal depression than with other types of life events. Other cross-sectional studies of antenatal depression using the LTE-Q have found unemployment, bereavement of a close person, serious problems with a friend or relative and moving house in the last 12 months to be significant predictors in univariable analyses, but not in multivariable analyses after controlling for social support and obstetric factors (Agostini et al., 2015).

Relationship breakdown and serious financial problems are both life events that threaten a woman's emotional and physical security at a crucial point in her life and, therefore, it is not surprising that these types of life events were significantly associated with depression symptoms cross-sectionally in this study. Theories of a woman's transition to motherhood suggest that a supportive partner is extremely important in buffering a woman from the stresses of becoming a mother (Figueiredo et al., 2008) and helping a woman to successfully negotiate changes in her sexuality, personal relationships and responsibilities (Nicolson, 1999). Conversely, a difficult relationship can also be a serious stressor that impacts negatively on a woman's mental health. Antenatal and postnatal depression is associated with poor partner relationship quality and lack of perceived social support from the partner (e.g., Yim et al., 2015).

A lack of a stable partner who can assist in helping to raise a child also increases the physical and emotional demands that a woman has to deal with which in itself may trigger depression. Parental stress and perceived maternal competence are associated with depression in mothers (Leigh & Milgrom, 2008). Thus, difficulties in the partner-relationship could represent both a stressor and a vulnerability factor in the stress-diathesis model of depression.

Having a child has serious financial implications for a woman as it can be difficult to maintain employment during pregnancy and secure work after childbirth, on top of the costs of providing for a child materially. Financial pressures can also be related to breakdown in partner relationship if, for example, a woman loses the income of her partner. Financial difficulties may threaten the physical well-being of a mother and her child directly, and therefore, is likely to be perceived as highly threatening. Life events that are severe and have long-term ramifications have been theorised to be the most depressogenic (Brown & Harris, 1978). Financial stressors during the perinatal period are also occurring at a time when a woman has limited opportunity to address her financial situation directly because of her pregnancy or childcare responsibilities. Adverse circumstances which are outside of a person's immediate control can lead to learned helplessness and hopelessness characteristic of depression (Abramson, Seligman & Teasdale, 1978) and make it harder to engage in problem-focused coping (Lazarus & Folkman, 1984).

In the present study, both unemployment and serious financial problems at 1 year postnatal were associated with depression in univariable analyses, but only serious financial problems remained an independent predictor when the life events were adjusted for each other. One reason for this may be that unemployment does not significantly explain any further variance in the current regression model than that already explained by serious financial problems. However, it does highlight the fact that negative life events often naturally co-occur because of the impact one may have on the other, with the result that they may not remain as independent significant predictors in multivariable analyses. For that reason, it is equally important to pay attention to significant factors in univariable, unadjusted analyses, as well as multivariable analyses, when considering public health interventions for identifying and helping at-risk populations (Holzmann et al., 2006).

Notably, Liu and Tronick (2013) examined different combinations of life events that particularly increased the risk of postnatal depression in cross-sectional analyses and found that the presence of financial stress was a common denominator in all of the combinations that predicted an increase in risk. Indeed, women who experienced high levels of partner conflict and family health problems but who did not have financial difficulties were not at an increased risk. It is perhaps not surprising that financial problems would contribute towards significant distress in the postnatal period given the increased financial burden of having a child and potential difficulty returning to work.

In this study, relationship and financial types of events did not continue to be independent predictors of perinatal depression when adjusted for comorbid anxiety and somatic symptoms, although relationship breakdown at 26 weeks pregnancy approached significance in the full multivariable model (OR 10.3, CI 1.00-105.99, $p = 0.050$). This is similar to studies in the general population that have also controlled for comorbid clinical disorders with depression. A large general population study of men and women with experience of depression or anxiety ($N = 2288$) found that life-time experiences of bereavement, health difficulties, relationship breakdown and close interpersonal problems (as assessed on the LTE-Q) were significantly associated with lifetime diagnoses of depression when controlling for demographics but not when controlling for current comorbid disorders such as anxiety (Spinhoven et al., 2010). The only predictors that remained significant after controlling for comorbid disorders were childhood neglect or abuse.

Prospective associations.

The prospective analyses revealed that having a serious problem with a close friend, relative or neighbour during pregnancy was a significant predictor of postnatal depression in both prospective models (life events experienced during early to late pregnancy, and life events experienced during late pregnancy to the early postnatal period) after adjusting for age, deprivation and antenatal depression, anxiety and somatic symptoms. This finding highlights the long-term vulnerability for the development of depression that a lack of social support confers on women. The ability of social support to moderate the impact of life stress (the "stress-buffer" hypothesis; Cohen & Wills, 1985) is well established in the perinatal depression literature as having a moderate protective effect (O'Hara, 2009; Robertson et al., 2004). Nevertheless, poor social support may also represent adverse circumstances in itself for women during the perinatal period which may directly contribute to depression symptoms (Brugha, 1990).

Life events may have direct and indirect effects on depression and several studies have conducted path analyses using multiple regression to map out the indirect pathways that life events lead to perinatal depression. One indirect pathway to depression is that life events result in an increased need for partner and social support which, in the absence of adequate support, increases the risk of depression (Bernazzani, Saucier, David, & Borgeat, 1997; Glazier et al., 2004; Zelkowitz et al., 2004). This may be one reason why some studies have found that the significant relationships between life events and perinatal depression symptoms in univariable analyses become non-

significant after controlling for the impact of social support in multivariable analyses (e.g., Agostini et al., 2015; Zelkowitz et al., 2004).

Various aspects of social support have been investigated but perceived social support (the belief that support is available if needed) from a woman's partner is among the strongest protective factors (Yim et al., 2015). Conversely, lower levels of perceived social support and poorer partner relationship quality act as risk factors for postnatal depression (Yim et al., 2015).

Research regarding women's experiences of transitioning to motherhood suggests that having the support and advice of other mothers who can empathise with the experience of becoming a mother and provide reassurance is important to a woman's transition (Staneva, Bogossian, & Wittkowski, 2015). Martell (2001) described first-time mothers' experiences of orienting themselves to motherhood after childbirth and reported women feeling more connected to their mothers, mothers-in-law and other women as a result of their psychosocial development. Qualitative research has identified recurring themes in women's reported experiences of perinatal depression which revolve around struggles with living up to maternal ideals, social and emotional isolation and loss of self (Mauthner, 2010; Nicolson, 1999). The absence of social support from a woman's friends and family may make it more likely that cognitive processes such as rumination and worry regarding these salient issues for women in the perinatal period go 'unchecked' and lead to depression.

Interestingly, in this study, serious problems with a close friend, relative or neighbour during pregnancy (types of life events; prospective model i, OR 2.8, model ii OR 3.7) had a similar strength of association with postnatal depression as did antenatal depression (OR 2.5-2.7 across all models) and antenatal somatic symptoms (OR 2.4 across all models) across both prospective models (i and ii). Antenatal anxiety emerged as the strongest predictor of postnatal depression in the prospective analyses which is consistent with the literature on anxiety being a significant predictor of depression, both antenatally and postnatally (Coelho et al., 2011; Prenoveau et al., 2013; Skouteris et al., 2009). Recent dimensional models of depression, anxiety and somatic symptoms (SAD triad) posit a symptom overlap stemming from a broad common psychological distress factor (Simms et al., 2012). However, Simms et al.'s (2012) dimensional model of the SAD triad does not account for possible directionality between disorders or why the present study, and others (Matthey et al., 2003), have found antenatal anxiety to be a stronger risk factor for postnatal depression than antenatal depression.

In the postnatal period, early anxiety has been found to be a better predictor of later comorbid depression and anxiety than earlier depression (Prenoveau et al., 2013) and comorbid perinatal anxiety and depression is associated with a greater functional impairment, severity and duration of depression symptoms (Rowe et al., 2008). Therefore, one possibility is that antenatal anxiety is a stronger predictor of postnatal (comorbid) depression symptoms that are severe enough to be above the clinical cut-off postnatally in this study. On the other hand, antenatal depression symptoms may be more strongly associated with postnatal depression symptoms (without anxiety) that are more likely to diminish postnatally below the clinical cut-off. Nevertheless, it is generally accepted that anxiety is often a precursor to depression, although the causal mechanisms are still to be identified (Wittchen, Kessler, Pfister, & Lieb, 2000).

Study strengths and limitations

Design.

To the author's knowledge, the present study is the first to examine the cross-sectional and prospective associations between the number and type of life events on depression across the perinatal period, whilst controlling for comorbid anxiety and somatic symptoms in a large population cohort study. A key strength of this study is the prospective design in which assessments of the exposure (life events) were undertaken before the outcome (depression) occurred. This avoids retrospective recall bias which can lead to people reporting more past adversity or reflecting differently on adversity when they are currently experiencing depression symptoms (Ben-Zeev, Young, & Madsen, 2009). Nevertheless, issues with recall bias are also relevant to some prospective designs where there is a possibility that onset of the outcome could have occurred before the exposure between periods of assessment (Hassan, 2006). However, this type of recall bias is known to effect the retrospective recall of meaning, cognitions and affect regarding past adversity (Ben-Zeev et al., 2009), none of which were investigated in this study. The recall of whether or not major life events have recently occurred is relatively more objective and less likely to be affected by recall bias (Kendler et al., 2002).

It is possible that depression symptoms preceded life events in the cross-sectional analyses in this study because we do not have an indicator of when depression symptoms started to occur. Therefore, some life events may not have been involved in the onset of depression symptoms, although there is evidence to suggest that concurrent

life events exacerbate or maintain depression symptoms in the perinatal period (Fisher et al., 2013; Husain et al., 2012; Keers et al., 2010). Nevertheless, the prospective analyses were able to examine the strength of association between life events occurring during pregnancy and postnatal depression.

Future research aiming to test causal processes more directly would require more intensive methods of data collection such as the use of interview schedules (e.g., LEDS) or diary study methodologies that could track the timing of events and depression symptoms over time. The timing of events is critical to determining their aetiological role in depression onset (Spence et al., 2015). Nevertheless, these methods are expensive and not feasible for large scale population studies.

A limitation concerning the timing of life events and mental wellbeing assessment in this study is that the life events captured at 8 weeks postnatal may contain some life events also captured at 26 weeks pregnancy because of the four-week overlap between them (see Figure 1 in *Method*). However, this did not present any issues for the analysis because the logistic regression models did not use life events data from both 26 weeks pregnancy and 8 weeks postnatal simultaneously in one model. Moreover, this does not affect interpretations of individual regression models because each model tests the association between life events in the previous six months on either concurrent or later perinatal depression symptoms. In addition, the timing of assessment also resulted in an 18-week gap between assessment at 8 weeks postnatal and 1 year postnatal where life events were not assessed (see Figure 1 in *Method*). Therefore, it is possible that depression at 1 year postnatal was associated with life events not captured in the present study.

The main limitation with regards to the study design were the lack of available data on other important demographic and psychosocial variables that have previously shown associations with perinatal depression including history of depression and anxiety, measures of social support, perceived stress, chronic stressors, obstetric factors and cognitive factors that impact upon resilience (Biaggi et al., 2016; Yim et al., 2015). Some of these factors may have moderated the relationship between life events and depression (Yim et al., 2015). Their absence in the multivariable models means that the association between life events and depression found in the present study may be a proxy for other relationships between variables such as perceived stress and perinatal depression (Kingston, Tough, & Whitfield, 2012). In addition, psychological factors such as measures of coping, resilience, the maternal bond in utero and postnatal and maternal attitudes regarding motherhood have been shown to increase the risk of

depression during the perinatal period (Biaggi et al., 2016). Sockol et al. (2014) found that specific negative beliefs about motherhood that are activated by parental stressors could mediate the relationship between these stressors and the emotional response to it.

However, the BaBY study from which these data were taken was not designed with the intention of specifically examining the relationship between life events and perinatal depression but rather, it is a long-term study interested in the health and wellbeing of babies and their parents.

As a history of depression was not available for the women in this study, it is also not known whether "new" cases of postnatal depression onset were first episodes of depression or a recurring episode with onset prior to pregnancy. Stressful life events may have a stronger relationship with first episodes of depression than recurrent episodes (Kendler, Thornton, & Gardner, 2000). However, life events of a moderate or minor severity have been shown to be more prevalent in recurrent than in first episodes of depression (Roca et al., 2013).

Participants.

This study collected data from the general population in Yorkshire which increases the generalisability of these findings to other women of child-bearing age in the general population. However, the majority of women in this study were between 30-40 years old and lived in areas of relatively little deprivation and, therefore, are not fully representative of the UK perinatal population.

The main limitation of this study was that complete data was only available for 907 out of 2382 women who initially returned some data at the first time point in the study (26 weeks pregnancy). Participant attrition is a common methodological problem in longitudinal studies and attrition rates between 30-70% have been reported elsewhere (Gustavson, von Soest, Karevold, & Røysamb, 2012). Participant attrition is rarely completely random and, therefore, can introduce bias into the study if the group that is lost to follow up is different to the group that completes the study (Dumville, Torgerson, & Hewitt, 2006). Examination of differences between the complete and incomplete cases of women at baseline (26 weeks pregnancy) in this study showed that the incomplete sample had a significantly greater proportion of women scoring above the clinical cut-off for symptoms of depression (11.7% versus 7.3%), anxiety (15.7% versus 9.5%) and somatising (31.9% versus 26.2%) as well as experiencing significantly more life events on average (0.5 versus 0.3). Previous studies have found null associations or weak-to-moderate associations between levels of higher

psychological distress and attrition in population cohort studies (Bjerkeset, Nordahl, Larsson, Dahl, & Linaker, 2008; de Graaf, Bijl, Smit, Ravelli, & Vollebergh, 2000; Eaton, Anthony, Tepper, & Dryman, 1992; Tambs et al., 2009).

The incomplete sample in this study is a heterogenous group of women who may have returned between one and eleven questionnaires out of the possible twelve questionnaires in the entire study. Therefore, limited assumptions can be made about reasons for non-response in this group of women. Nevertheless, it is possible that analyses based on the complete cases in this sample has led to an underestimation of the effect of life events on perinatal depression if women who became depressed following a number of life events then did not respond to further questionnaires in the study.

Measures.

The use of self-report measures of depression, anxiety and somatic symptoms in this study may have led to inflated estimates of prevalence or comorbidity given that estimates are generally lower when clinical diagnoses have been used (Woody et al., 2017). Moreover, the question has been raised as to whether life events show stronger associations with depression when measured by symptom screening tools than clinical diagnoses (Yim et al., 2015). The absence of clinical diagnoses of depression and anxiety in this study means that there is the potential that the symptom checklists used for anxiety and depression are tapping into a similar construct, i.e. a broader perinatal distress construct that includes depression, anxiety and stress (Miller, Pallant & Negri, 2006). The importance of discerning depression and anxiety from each other during the perinatal period has been highlighted (Matthey et al., 2003). The strengths of using the PHQ-8 and GAD-7 is that they have been shown to capture distinct constructs in factor analysis (Kroenke et al., 2010), as opposed to a depression measure such as the Edinburgh Postnatal Depression Scale (EPDS) which additionally includes items capturing anxiety symptoms (Brouwers, van Baâr & Pop, 2001).

There is also the risk that participants may under-report psychological distress in mental wellbeing self-report measures because they perceive that to be socially desirable (Nederhof, 1985). Indeed, participants in this study were aware that one of the aims of the BaBY project was to collect information on the mental wellbeing of women during the perinatal period, and some participants may have been motivated to portray favourable adjustment to their pregnancy and motherhood. However, participants in this study were allowed to complete the measures privately and given assurances of anonymity which have been shown to reduce the risk of social desirability (Paulhus,

1984). Despite these limitations, self-report measures are widely used and represent affordable and feasible methods of collecting information from participants in acceptable ways (Haberer, Trabin, & Klinkman, 2013).

The self-report measures used in this study are valid measures of distress, with the PHQ-9 (from which the PHQ-8 is derived) and GAD-7 selected by commissioners and clinicians as appropriate screening tools for use in primary care in the UK (Kroenke et al., 2009). However, there are limitations to the measures used in this study. Primarily, the PHQ-8, GAD-7 and PHQ-15 are designed to be symptom screening tools which give an indication about the severity of symptoms based on predefined clinical cut-offs (Kroenke et al., 2010). Nevertheless, they do not give an indication of the level of distress or functional impairment these symptoms cause, both of which are requirements of a DSM-V clinical diagnosis of major depression (APA, 2013). Moreover, they also rely on participants making correct attributions of ambiguous symptoms (Haberer et al., 2013) which, during pregnancy, may be complicated by normal physiological changes (Simpson et al., 2014). Relating to this, it is possible that the somatic symptom measure used in the present study (PHQ-15) captured a mixture of somatic symptoms relating to normal physiological processes involved in pregnancy and the early postnatal period as well as to psychological distress.

There are some proponents of the view that screening measures of depression during pregnancy should not include any somatic symptoms of depression which could be conflated with physiological changes due to pregnancy (Yonkers et al., 2009). However, McMahon et al. (2017) found that the only item on the PHQ-8 endorsed more frequently by pregnant women than women in the general population with minor depression was changes in energy levels. Their overall recommendation is that somatic items are kept in the PHQ-8 as they are valid indicators of depression and that clinicians should explore attributions of this item, in particular, further with pregnant women where necessary.

One limitation of the LTE-Q that was demonstrated in the present study was that a minority of participants (6%) reported life events outside of the specified previous six-month period even though this was clearly stated in the measure. The potential for this to occur has been acknowledged in the literature (e.g., Patton, Coffey, Posterino, Carlin, & Bowes, 2003) although, to the author's knowledge, suggestions to remedy this have not been put forward. Including events that have happened in the distant past is likely to lead to biased associations between recent life events and the development of depression. Asking participants to report dates of life events on the LTE-Q and

excluding events preceding the time period may be one solution to preserving the validity of the LTE-Q, as was done in the present study. Other improvements to the LTE-Q have also been suggested. One study asked participants to appraise events that occurred on the LTE-Q as positive, neutral or negative (Patton et al., 2003). Appraisal of events was found to be a significant moderator, with positive or neutral appraisal reducing the risks of developing subsequent depression.

Finally, as noted in the *Method* chapter, the item relating to problems with menstruation on the PHQ-15 is problematic for the perinatal population where there are a variety of normal biological factors that affect menstruation. One solution may be to exclude the item in studies of the perinatal period (Kelly et al., 2001; Senturk et al., 2012) in the same way that studies investigating somatic symptoms in men have done (e.g., Hinz et al., 2017). In this study, it was decided to keep the menstruation item as some women at 1 year postnatal did report problems in this area (see Method chapter for further details). Missing responses to this item at 8 weeks postnatal and 1 year postnatal were assumed to be missing because women had not yet had their menstruation cycle return due to normal physiological processes related to breastfeeding. Missing responses were, therefore, re-coded as '0' (not at all a problem). A possible consequence of treating missing answers to the menstruation item in this way (i.e. re-coding as a score of '0' instead of counting it as a missing item) is that more women may have been included in the complete case sample than if non-response to this item counted as a 'missing item'. Indeed, two cases were excluded from the complete case sample because the PHQ-15 contained missing items that exceeded 20% of the total number of items.

Analysis.

The present study used logistic regression models to examine associations between life events and perinatal depression in univariable and multivariable analyses. A strength of the present study is that it controls for symptoms of comorbid clinical disorders in the multivariable analyses. Few studies of perinatal depression have controlled for clinical comorbidity despite the fact that depression, anxiety and somatic disorders are highly comorbid and that anxiety, in particular, is a strong risk factor for general and perinatal depression, (Pulawski et al., 2017). It is important to account for the effects of clinical comorbidity given that evidence suggests that life events differentially impact the development of anxiety and depression (Kendler et al., 2003 Marteinsdottir et al., 2007).

The descriptive results in this study highlight the fact that perinatal mental health is not fixed but varies over time in relation to a person's circumstances. They also confirm the findings of previous studies showing the transient nature of some depression symptoms (Matthey & Ross-Hamid, 2012; Ballestrem et al., 2005) and the different groups of depression and anxiety symptom trajectories across the perinatal period (Bayrampour et al., 2016). It is important to note, however, that logistic regression models are fixed in their nature and cannot capture the complexity of continuously changing symptom trajectories during the perinatal period. Therefore, what is not explicit in the series of cross-sectional and prospective models in this study is that there are likely to be different groups of women in the "depressed" category across each of the models.

Post-hoc model fit analysis revealed that the majority of the regression models were found to fit the data relatively well, and when they did not, removal of cases that had large influences on the model resulted in satisfactory model fit in all but one of the models (the model relating to types of life events at 8 weeks postnatal). Results of these models, therefore, need to be interpreted with caution.

As has already been highlighted, few studies have prospectively examined the relationship between risk factors in pregnancy and postnatal depression by distinguishing between depression that has its onset during pregnancy and that which has its onset postnatally (Verrealt et al., 2014). It is possible that the different groups of depression and anxiety symptom trajectories identified by Bayrampour et al. (2016) (e.g., persistent sub-clinical depression, postnatal symptoms only) have different associations with life events. Due to the small numbers of women in this sample experiencing depression postnatally, it was not possible to examine differences between groups of women with persistent depression and postnatal onset only because the analysis would be underpowered (see *Results* chapter). The groups were combined in the prospective analyses and the effects of life events on postnatal depression were adjusted for the increased risk conferred by depression during pregnancy. Importantly, however, the results of the initial exploratory model investigating the prospective association between life events and postnatal depression onset revealed very similar associations (in terms of reported OR and CI) to the prospective models in the present study which used any postnatal depression (regardless of antenatal or postnatal onset) as the outcome. See Appendix I for results of the sensitivity analysis showing the results of the exploratory model examining life events as predictor of postnatal depression onset.

In addition, it was also not possible to separately examine associations with postnatal depression at 8 weeks and 1 year postnatally, and the groups were combined to improve the power of the analysis. It is possible that life events during pregnancy may have had stronger or weaker associations with depression at 8 weeks or 1 year postnatal but these associations were masked by combining the two time-points. However, to the author's knowledge, there has been no indication in the literature that depression at 8 weeks and 1 year postnatal are aetiologically different from each other. Furthermore, the low number and range of life events reported in this sample meant that life events were dichotomised in the analysis as either none or one or more life events. Although significant associations with perinatal depression have been found in studies using the same dichotomisation, other studies have found that an association only existed between a greater number of life events and depression. Life events have been shown to have a dose-response relationship with perinatal depression (eg. Stone et al., 2015), as well as confer increased risk if they are spread over multiple, rather than single, life domains (Liu & Tronick, 2013); however, the limited range in number of life events reported in this sample meant that these relationships were not able to be explored in greater detail. Moreover, there is always a loss of information associated with dichotomising continuous scores such as with the well-being scores in the present study. As a result of using categorical data, it is impossible that changes in "caseness" were sometimes due to the unreliability of the measure, rather than reflecting meaningful changes in clinical presentation (Jacobson & Truax, 1991). One alternative to using cut-off scores as indicators of clinical change is to use criteria for clinical and reliable change which ensures that the size of change in scores from above the cut-off to below the cut-off is greater than the level of change that is due to the inherent unreliability of the measure (Jacobson & Truax, 1991). For example, McMillan, Gilbody and Richards (2010) demonstrate the calculation of a reliable change index to be used with the PHQ-9.

The aims of the study were to investigate whether life events predicted increases in perinatal depression symptomatology to a severity that would warrant further clinical assessment and treatment. Therefore, clinical cut-offs that indicated a moderate severity of symptoms were used to dichotomise women into symptomatic and non-symptomatic groups. However, the limitation of dichotomising data in this way is that information is lost about the variation of women in each of the groups. For example, it is likely that the non-depressed group (PHQ-8 score <10) contained women with a mixture of mild and

sub-clinical depression symptoms, some of which may have been associated with life events. Nevertheless, logistic regression models using clinical cut-offs of moderate symptom severity to dichotomise the data are widely used in perinatal depression research (e.g., see Milgrom et al., 2008, Oppo et al., 2009 as examples of large, prospective studies).

Clinical implications

Assessment of risk factors for perinatal depression.

The findings of this study have important implications for the assessment and identification of women during the perinatal period who may be vulnerable to experiencing depression symptoms. The perinatal period provides a particularly large number of opportunities for health professionals to come into contact with women in which assessment and intervention of depression symptoms can be proactively addressed (BPS, 2016). The findings of this study show that the presence of life events throughout the perinatal period increases the risk of depression but that greater vulnerability is conferred by problems in relationships with partners and close friends, as well as financial problems. Women should be asked during their routine healthcare appointments throughout pregnancy and the early postnatal period about their current and recent life circumstances as well as the meaning and ongoing consequences of any major life events. Though not a part of the present study, research also suggests that life events occurring in a woman's partner's life also have an impact on their wellbeing (Divney et al., 2012).

Importantly, assessment of a woman's potential vulnerability to developing perinatal depression should also incorporate, as much as possible, the range of risk and protective factors that are evidenced to be associated with the development of perinatal depression. These include having a history of depression or anxiety, current comorbidity, history of childhood abuse, levels of perceived stress, levels of social support, quality of partner relationship, views towards pregnancy and past difficulties in childbirth (Bayrampour et al., 2016). At the minimum, assessment of psychiatric history, current life circumstances, wellbeing and level of social support is likely to benefit many women (Milgrom et al., 2008).

Depression screening.

Whilst no screening measure of postnatal depression has been yet identified as the 'gold standard', a recent review comparing self-report depression measures found that they performed comparably with each other in detecting postnatal depression (Ukatu et al., 2018). Notably, the two item Patient Health Questionnaire (PHQ-2; Kroenke et al., 2003) had the highest sensitivity of all screening measures, ranging from 62% (specificity 79%) (Smith, Gotman, Lin, & Yonkers, 2010) to 100% (specificity 79.3%) (Chae, Chae, Tyndall, Ramirez, & Winter, 2012), showing that ultra-brief screening tools are available for health professionals under time pressure. In addition, some researchers have suggested than screening for perinatal depression should take place at several points during pregnancy (Biaggi et al., 2016) and during the first year post childbirth (Smith et al., 2016), arguing that diagnosing perinatal depression is difficult if screening only takes place once during pregnancy and after childbirth. Nevertheless, pregnancy in itself can cause temporary emotional distress. A study has shown that 66% of women with moderate depression symptoms attributed a significant number of symptoms as being pregnancy-, rather than mood-, related (Matthey & Ross-Hamid, 2011). Therefore, it can be helpful to explore the attributions of symptoms with women who score highly on depression measures as well as conduct a repeat administration of a depression screening measure a few weeks later, given the transient nature of some symptoms of perinatal distress (Matthey & Ross-Hamid, 2012).

A recent systematic review reported significant benefits of depression screening programmes during pregnancy and the postnatal period, including a reduction in prevalence of depression and better rates of remission and treatment response in postnatal women (N = 11,869) (O'Connor et al., 2016). However, these screening programmes were often accompanied by additional interventions such as care coordination or provision of counselling, and, therefore, the authors could not always disentangle the benefits of screening from the benefits of interventions. In addition, the cost-effectiveness of the screening programmes was not examined.

In the UK, universal screening for perinatal depression has not been recommended based on a lack of evidence that screening is cost-effective and leads to interventions that improve mother and child outcomes (Hill, 2010). However, NICE guidelines have recommended that healthcare professionals should be alert to the possibility of depression and comorbid mental health difficulties during the perinatal health period and enquire about symptoms when appropriate, particularly when a history of depression is known (NICE, 2007). In the US and Australia, screening for

perinatal depression is only recommended when a package of follow-up care can be provided (Austin & Highet, 2011; Siu et al., 2016).

Role of clinical psychology.

The integral role of clinical psychology in the delivery of perinatal mental health services was recently summarised in the 2016 British Psychological Society report (BPS, 2016). In this report, the ways in which clinical psychologists can provide the particular skills and leadership needed to facilitate the aims of the Five Year Forward View Implementation Plan for perinatal services were outlined. Clinical psychologists have specialist skills in clinical leadership, supervision, teaching, training and service development, alongside direct therapeutic skills. Assessment of perinatal depression is likely to be undertaken by healthcare professionals who already have routine contact with women during pregnancy and in the postnatal period. These healthcare professionals would benefit from training and supervision by clinical psychologists regarding conducting holistic assessments of women's life circumstances and experience of distress during the perinatal period within the context of a patient-centred consultation (Littlewood et al., 2016).

The priority is to deliver perinatal mental health services that are accessible, promote engagement with service users, combat stigma and deliver evidence-based therapeutic interventions (NHS England, 2016b). This is important given that women have shown a clear preference for psychological support as opposed to pharmacological interventions during the perinatal period for mental health difficulties (Buist, O'Mahen & Rooney, 2015). Timely and effective interventions reduce the risk of chronic mental health problems developing that require more costly and intensive treatments (Falah-Hassani et al., 2016).

Crucially, psychological interventions targeted at modifying psychosocial risk factors that play an important role in increasing or decreasing the risk of depression during the perinatal period are needed. Depression has been considered a psychological disorder arising from emotional regulation difficulties (Malik, Wells & Wittkowski, 2015). Poor cognitive coping strategies such as rumination has been linked with maintaining episodes of depression and negative affect (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008). Other cognitive models of depression suggest that depression arises from dysfunctional schemas about the self which can be targeted through cognitive therapies of depression (Beck et al., 1979). In addition, behavioural models of depression highlight how behavioural changes that are part of the depressive response

serve to maintain other depression symptoms (Jacobsen et al., 1996). For example, behaviours such as withdrawal or avoidance may initially provide short-term relief through reducing demands on an individual who is feeling low in mood. However, these behaviours then provide less opportunities for positive, meaningful activity for the person to engage in feeds a vicious cycle of depression symptoms (Jacobsen et al., 1996). Behavioural activation is a brief and evidence-based treatment that promotes positive behaviours and activities which provide positive reinforcement to the individual with the aim of boosting mood, confidence and energy (Ekers, Richards & Gilbody, 2008.

A recent meta-analysis has found that psychological interventions for perinatal depression significantly reduced depression symptoms to below that of a clinically significant level and showed similar efficacy to psychological interventions for depression in the general population (Sockol, Epperson, & Barber, 2011). Interestingly, studies of therapies with an interpersonal focus (such as Interpersonal Psychotherapy, IPT) had significantly larger effect sizes (Hedge's $g = 0.96$) than studies of therapies with a cognitive-behavioural focus (such as Cognitive Behavioural Therapy, CBT) (Hedge's $g = 0.40$), although there were no head-to-head comparison studies (Sockol et al., 2011). This finding has been previously reported in the literature (Bledsoe & Grote, 2006) and may reflect the greater disruption to interpersonal relationships that are brought on by pregnancy and motherhood (Stuart & O'Hara, 1995). Similarly, interventions for women who are "at-risk" (currently not symptomatic) that have specifically focused on increasing social support from significant members of a woman's social network and from relevant professionals have shown some effectiveness (Fraser, Armstrong, Morris, & Dadds, 2000).

In addition, recent research has demonstrated moderate associations between mothers' and fathers' depression symptoms postnatally, with the strongest risk factor being parenting stress (Anding, Röhrle, Grieshop, Schücking, & Christiansen, 2016). This suggests that couple interventions addressing depression symptoms and parenting stress may be helpful.

Areas for further research

Further research is needed using large, prospective, population cohort designs that capture detailed information about life events and ongoing difficulties as well as capturing information on a range of important risk and protective factors that have already been identified in the literature. Larger numbers of complete cases would enable

additional exploration of how life events are associated with different groups of perinatal depression symptoms (antenatal versus postnatal onset) (Verreault et al., 2014), as well as factors that moderate the relationship between life events and depression, such as chronic stress (Yim et al., 2015). In addition, it is possible that a more nuanced conceptualisation of life events and stress would show stronger associations with perinatal depression. Liu and Tronick (2013) investigated the pattern of life events as a predictor of postnatal depression. They found that life events occurring in particular combinations of life domains were the strongest predictors and associated with the greatest risk of depression after adjusting for demographic variables compared with numbers of life events or individual types of life events as predictors. This is an interesting finding that warrants further research.

Capturing contextual information about life events from checklist methods has not been possible thus far. However, a new digital online technology known as the Computerised Life Events Assessment Record (CLEAR) is currently being developed based on the LEDS (Spence et al., 2015). The online assessment tool would use calendar-based timing to assess life events and difficulties in the participant's life and that of close others, similarly to the LEDS. In this way, it would allow in-depth life events data to be collected using cost-effective survey methods which has so far only been possible through resource-intensive interview schedules.

Emerging evidence has also highlighted that depression and anxiety are also common in men during the perinatal period (Darwin et al., 2017) and that comorbidity exists within couples (Anding et al., 2016). One meta-analysis found a moderate association between maternal and paternal depression in the perinatal period (Paulson & Bazemore, 2010) but studies have not yet explored partner mental health difficulties as a risk factor. Future research is needed to understand how mental health difficulties in womens' partners impact their own vulnerability to perinatal distress and vice versa (Leach et al., 2017).

A developmental model of perinatal depression is needed that integrates the extensive empirical evidence base for risk factors for general depression along with particular risk factors that are significant for perinatal depression including obstetric and psychosocial risk factors. Kendler et al.'s (2002) empirically derived developmental model of general depression describes several pathways to the development of depression including an "adversity" pathway. The adversity pathway includes marital problems as the only particular life event in the last year associated with depression onset. However, in this study, serious problems with a close friend or relative was the

only life event during pregnancy that predicted associations with postnatal depression, and independently of antenatal depression, anxiety and somatic symptoms. Future research may identify that a lack of social support is a stronger risk factor for perinatal depression than depression at other times in a woman's life. Evidence from women's qualitative accounts suggest that peer support (Jones, Jomeen, & Hayter, 2014) and opportunities for validation from other women who have shared experiences is particularly key to dealing with distress in the perinatal period (Staneva, Bogossian, & Wittkowski, 2015).

Conclusion

This is the first UK-based population cohort study which has explored the association between life events and perinatal depression, whilst controlling for comorbid anxiety and somatic symptoms. These associations were explored using a series of cross-sectional and prospective logistic regression models. Cross-sectional models investigated the strength of association between recent life events and current depression symptoms during pregnancy and the postnatal period. Prospective models investigated associations between life events during pregnancy and depression in the postnatal period. Consistent with a stress-vulnerability model of depression, life events have been shown to increase the vulnerability of women experiencing depression symptoms during the perinatal period. In particular, specific types of life events such as relationship breakdown and serious financial problems were associated with higher odds of perinatal depression symptoms than the number of life events alone, and were also shown to be more consistent predictors. Specific life events were also more consistent predictors of postnatal depression in prospective analyses than the number of life events alone.

Life events did not tend to independently predict depression after adjusting for comorbid anxiety and somatic symptoms, of which anxiety was consistently the strongest predictor of depression across the perinatal period. The results of this study highlight the increased risk of postnatal depression when antenatal depression, anxiety or somatic symptoms are present. Further, perhaps the most important finding is that serious problems in a woman's social network (close friends and relatives) that occurred during pregnancy and soon after childbirth increased the risk of postnatal depression independently to higher antenatal depression, anxiety and somatic symptoms. It is hoped that the findings of this study will inform public health policy and clinical

practice in advancing better prevention, detection and treatment of women experiencing emotional distress during the perinatal period.

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Appendix A:
Ethical Approval Letter for BaBY study

Health Research Authority
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25 April 2013

Liz Littlewood
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Dear Liz

Study title:	**Born and Bred in Yorkshire: A Hull York Medical School Family Study**
REC reference:	**11/NE/0022**
Protocol number:	**N/A**
Amendment number:	**Amendment 3**
Amendment date:	**26 March 2013**
IRAS project ID:	**64150**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a **favourable ethical opinion** of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Protocol	BABY Protocol - Version 2	13 March 2013
Notice of Substantial Amendment (non-CTIMPs)	Amendment 3	26 March 2013

Covering Letter		03 April 2013
BABY Detailed List of Revisions (Amendment 3)		13 March 2013
BABY Family Details Form	Version 2	13 March 2013
Participant Information Sheet: BABY Parent	Version 3	13 March 2013
Protocol	BABY PaNDA Protocol Version 1	11 March 2013
Letter of invitation to participant	BABY PaNDA Version 1	11 March 2013
Participant Consent Form: BABY PaNDA	Version 1	11 March 2013
Participant Information Sheet: BABY PaNDA	Version 1	11 March 2013
BABY PaNDA Letter to GP: notification of risk of depression/anxiety	Version 1	11 March 2013
BABY PaNDA letter to GP: notification of risk	Version 1	11 March 2013
BABY PaNDA Letter to GP: informing of consent	Version 1	11 March 2013
BABY PaNDA Cover Letter: 1 Year Follow-up	Version 1	11 March 2013
BABY PaNDA: NICE ultra-brief screening questions	Version 1	11 March 2013
Questionnaire: EPDS Questionnaire		
Questionnaire: BABY PaNDA: Biographical Questionnaire	Version 1	11 March 2013
CIS-R description		
Questionnaire: EQ5D		
Questionnaire: SF-12		
Questionnaire: PHQ-15		
Questionnaire: GAD-7		
Questionnaire: PHQ-9		
BABY PaNDA: Acceptability Survey (Postnatal)	Version 1	11 March 2013
BABY PaNDA: Acceptability Survey (Prenatal)	Version 1	11 March 2013
Questionnaire: BABY PaNDA: Resource-use Questionnaire (Postnatal)	Version 1	11 March 2013
Questionnaire: BABY PaNDA: Resource-use Questionnaire (Prenatal)	Version 1	11 March 2013
BABY PaNDA	Letter from funder	20 July 2012
BABY PaNDA: Topic Guide for Health Professionals	Version 1	11 March 2013
BABY PaNDA: Topic Guide for Participants	Version 1	11 March 2013
Participant Consent Form: BABY PaNDA Health Professionals	Version 1	11 March 2013
Participant Information Sheet: BABY PaNDA Health Professionals	Version 1	11 March 2013

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance
The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

11/NE/0022:	**Please quote this number on all correspondence**

Yours sincerely

pp

Dr Giles McCracken Chair

E-mail: nrescommittee.northeast-york@nhs.net

Enclosures: List of names and professions of members who took part in the review

NRES Committee North East - York

Attendance at Sub-Committee of the REC meeting via correspondence

Name	*Profession*	*Capacity*
Dr Giles McCracken (Chair)	Senior Clinical Lecturer	Expert
Dr John Newton	Social Scientist (Retired)	Lay Plus

Appendix B:
PHQ-8

Patient Health Questionnaire – 8 (PHQ-8)

Over the last two weeks, how often have you been bothered by any of the following problems? *(Use "✔" to indicate your answer)*	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	☐	☐	☐	☐
2. Feeling down, depressed, or hopeless	☐	☐	☐	☐
3. Trouble falling or staying asleep, or sleeping too much	☐	☐	☐	☐
4. Feeling tired or having little energy	☐	☐	☐	☐
5. Poor appetite or overeating	☐	☐	☐	☐
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	☐	☐	☐	☐
7. Trouble concentrating on things, such as reading the newspaper or watching television	☐	☐	☐	☐
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	☐	☐	☐	☐

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
☐	☐	☐	☐

Appendix C:
PHQ-15

Physical Symptoms (PHQ-15)

During the last four weeks, how much have you been bothered by any of the following problems? (*Use "✔" to indicate your answer*)	Not bothered at all	Bothered A little	Bothered A lot
1. Stomach pain	☐	☐	☐
2. Back pain	☐	☐	☐
3. Pain in your arms, legs, or joints (knees, hips, etc.)	☐	☐	☐
4. Menstrual cramps or other problems with your periods WOMEN ONLY – If pregnant not applicable	☐	☐	☐
5. Headaches	☐	☐	☐
6. Chest pain	☐	☐	☐
7. Dizziness	☐	☐	☐
8. Fainting spells	☐	☐	☐
9. Feeling your heart pound or race	☐	☐	☐
10. Shortness of breath	☐	☐	☐
11. Pain or problems during sexual intercourse	☐	☐	☐
12. Constipation, loose bowels, or diarrhoea	☐	☐	☐
13. Nausea, gas, or indigestion	☐	☐	☐
14. Feeling tired or having low energy	☐	☐	☐
15. Trouble sleeping	☐	☐	☐

Appendix D:
GAD-7

baby
born and bred in yorkshire

☐☐/☐☐☐☐☐/☐☐

Time Point (Delete as appropriate)
26 Weeks / 8 Weeks / 1 Year

GAD 7

Over the last two weeks, how often have you been bothered by any of the following problems? (*Use "✔" to indicate your answer*)	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	☐	☐	☐	☐
2. Not being able to stop or control worrying	☐	☐	☐	☐
3. Worrying too much about different things	☐	☐	☐	☐
4. Having trouble relaxing	☐	☐	☐	☐
5. Being so restless that it is hard to sit still	☐	☐	☐	☐
6. Becoming easily annoyed or irritable	☐	☐	☐	☐
7. Feeling afraid that something awful might happen	☐	☐	☐	☐

Appendix E:
LTE-Q

LTE-Q

The following is a list of important life events. For each life event please tick 'Yes' if you have experienced that life event over the last six months and 'No' if you have not. For those events that you have experienced, please also indicate the date that the event occurred with as much accuracy as you can.

	No	Yes	If Yes when did this occur?
1. You yourself suffered a serious illness, injury or an assault	☐	☐	D D / M M / Y Y
2. A serious illness, injury or assault happened to a close relative	☐	☐	D D / M M / Y Y
3. Your parent, child or spouse died	☐	☐	D D / M M / Y Y
4. A close family friend or another relative (aunt, cousin, grandparent) died	☐	☐	D D / M M / Y Y
5. You had a separation due to marital difficulties	☐	☐	D D / M M / Y Y
6. You broke off a steady relationship	☐	☐	D D / M M / Y Y
7. You had a serious problem with a close friend, neighbour or relative	☐	☐	D D / M M / Y Y
8. You became unemployed or you were seeking work unsuccessfully for more than one month	☐	☐	D D / M M / Y Y
9. You were sacked from your job	☐	☐	D D / M M / Y Y
10. You had a major financial crisis	☐	☐	D D / M M / Y Y
11. You had problems with the police and a court appearance	☐	☐	D D / M M / Y Y
12. Something you valued was lost or stolen	☐	☐	D D / M M / Y Y

Appendix F:
Data corrections and exclusions

1. Cases excluded because of unacceptable levels of missing items within measures

(a) PHQ-8
Note: Cases that had more than two items missing within the PHQ-8 were excluded from analyses
Number excluded: 2

(b) GAD-7
Note: Cases that had more than one item missing within the GAD-7 were excluded from analyses
Number excluded: 4

(c) PHQ-15
Note: Cases that had more than three items missing within the PHQ-15 were excluded from analyses
Number excluded: 2

(d) LTE-Q
Note: Cases that had more than one item missing within the LTE-Q were excluded from analyses
Number excluded: 2 (one of those cases had already been excluded due to being excluded from the PHQ-15)

1.1 Cases excluded because of erroneous completion

(a) LTE-Q: 1 case excluded

1.2 Total number of cases excluded from the complete case sample: 10

2. Cases corrected for missing items within measurse

Note: Missing items within the PHQ-8, GAD-7 and PHQ-15 were replaced with the mean score of the completed items, provided that the number of missing items did not exceed 20% of the total items. Missing items in the LTE-Q were recoded as 'No' (scored as 0) provided there was only one item missing.

Number of cases corrected:

PHQ-8
26 weeks pregnancy: 10
8 weeks postnatal: 4
1 year postnatal: 6

GAD-7
26 weeks pregnancy: 2
8 weeks postnatal: 1
1 year postnatal: 2

PHQ-15
26 weeks pregnancy: 46
8 weeks postnatal: 47
1 year postnatal: 11

LTE-Q
26 weeks pregnancy: 5
8 weeks postnatal: 5
1 year postnatal: 6

2.1 Total number of cases which had missing items corrected: 145

Appendix G:
Table 7.1 Stringent Multivariable Model 3.1

Table 7.1. Stringent multivariable logistic regression Model 3.1 for life events and depression symptoms at 8 weeks postnatal (depressed; *N* = 45; not depressed; *N* = 862)

	Unadjusted				Demographics				Clinical comorbidity			
		95% CI				95% CI				95% CI		
Variable	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value
Life events												
0	-				-				-			
≥1	2.05	1.05	3.993	0.035	1.96	0.996	3.856	0.051	1.4	0.61	3.40	0.402
Age (years)												
<20					6.7	1.274	35.26	0.025	2.3	0.22	23.93	0.481
21-30					2.18	1.102	4.32	0.025	3.4	1.40	8.15	0.007
31-40					-				-			
41-50					3.47	0.943	12.75	0.061	2.6	0.50	13.36	0.255
Deprivation					1.01	0.882	1.153	0.901	1.1	0.90	1.30	0.410
Anxiety												
No					-				-			
Yes									60.7	23.78	154.97	0.000
Somatising												
No					-				-			
Yes									3.4	1.34	8.58	0.010

Appendix H:
Table 8.1 Stringent Model 3.1

Table 8.1. Stringent multivariable logistic regression Model 3.1 for types of life events and depression symptoms at 8 weeks postnatal (depressed; *N* = 45; not depressed; *N* = 862)

	Unadjusted (Model 1)				Demographics (Model 2)				Clinical comorbidity (Model 3)			
		95% CI				95% CI				95% CI		
Variable	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value
Life events												
0					-				-			
≥1	2.0	0.25	15.89	0.508	1.8	0.21	14.81	0.593	2.8	0.27	30.03	0.388
Age (years)												
<20					(empty)				(empty)			
21-30					1.9	0.95	3.88	0.07	2.5	1.02	5.94	0.046
31-40					-				-			
41-50					3.4	0.92	12.55	0.068	2.2	0.43	10.91	0.349
Deprivation					1.1	0.91	1.22	0.514	1.1			
Anxiety												
No												
Yes									54.2	20.83	141.22	0.000
Somatising												
No												
Yes									3.9	1.50	10.10	0.005

Appendix I:
Sensitivity analysis of postnatal onset model

The sensitivity analysis showing the results of the initial exploratory model examining life events as predictor of postnatal depression that has its onset postnatally (N = 58).

Prospective associations between life events occurring during pregnancy through to the early postnatal period and postnatal depression were examined, with one model including life events during early to mid-pregnancy and a second, life events during mid-pregnancy to the early postnatal period (see *Method* chapter).

Prospective Model 1

(a) Presence of life events in early to mid- pregnancy.

	Unadjusted (Model 1)				Demographics (Model 3)				Antenatal Comorbidity (Model 4)			
	95% CI				95% CI				95% CI			
Variable	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value
Life events												
0	-				-				-			
≥1	1.5	0.84	2.79	0.163	1.4	0.76	2.60	0.28	1.3	0.67	2.38	0.462
Age (years)												
<20					7.8	2.07	29.10	0.002	6.2	1.52	25.20	0.011
21-30					1.1	0.63	2.00	0.699	1.1	0.58	1.90	0.868
31-40					-				-			
41-50					1.2	0.26	5.14	0.842	0.9	0.19	4.03	0.854
Deprivation					1.0	0.85	1.07	0.398	1.0	0.87	1.09	0.62
Antenatal Anxiety												
No									-			
Yes									2.9	1.46	5.91	0.003
Antenatal Somatising												
No									-			
Yes									2.0	1.11	3.66	0.021

(b) Type of life events in in early to mid- pregnancy.

	Unadjusted (Model 1)				Demographics (Model 3)				Antenatal Comorbidity (Model 4)			
	95% CI				95% CI				95% CI			
Variable	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value
Social/friendship problem												
No	-				-				-			
Yes	3.5	1.29	9.74	0.014	2.72	0.91	8.09	0.072	2.5	0.83	7.38	0.102
Age (years)												
<20					6.52	1.66	25.65	0.007	5.3	1.28	21.66	0.021
21-30					1.13	0.63	2.02	0.677	1.1	0.60	1.96	0.8
31-40					-				-			
41-50					1.22	0.28	5.37	0.795	0.9	0.19	4.12	0.874
Deprivation					0.95	0.85	1.06	0.368	1	0.87	1.09	0.594
Antenatal Anxiety												
No									-			
Yes									3	1.49	6.03	0.002
Antenatal Somatising												
No									-			
Yes									2	1.10	3.61	0.024

Prospective Model 2

(a) Presence of life events in mid-pregnancy to the early postnatal period.

	Unadjusted (Model 1)				Demographics (Model 3)				Antenatal Comorbidity (Model 4)			
	95% CI				95% CI				95% CI			
Variable	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value
Life events												
0	-				-				-			
≥1	1.9	1.08	3.40	0.026	1.81	1.01	3.24	0.046	1.7	0.94	3.08	0.082
Age (years)												
<20					7.91	2.11	29.69	0.002	6.2	1.53	25.33	0.011
21-30					1.11	0.62	1.99	0.714	1.1	0.58	1.92	0.856
31-40					-				-			
41-50					1.17	0.26	5.18	0.835	0.8	0.18	3.92	0.82
Deprivation					0.96	0.86	1.07	0.461	1	0.87	1.09	0.669
Antenatal Anxiety												
No									-			
Yes									2.9	1.45	5.87	0.003
Antenatal Somatising												
No									-			
Yes									2	1.11	3.65	0.021

(b) Type of life events in mid-pregnancy to the early postnatal period.

	Unadjusted (Model 1)				Demographics (Model 3)				Antenatal Comorbidity (Model 4)			
	95% CI				95% CI				95% CI			
Variable	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value
Social/friendship problem												
No	-				-				-			
Yes	3.6	1.37	9.46	0.009	3.4	1.25	9.00	0.016	3.9	1.41	10.51	0.008
Financial crisis												
No	-				-				-			
Yes	3.1	0.87	10.67	0.081	2.8	0.80	10.01	0.105	2.8	0.76	10.63	0.121
Age (years)												
<20					3.9	0.96	16.26	0.057	5.9	0.66	14.62	0.015
21-30					1.1	0.68	1.89	0.626	1.1	0.61	1.79	0.852
31-40					-				-			
41-50					1.0	0.29	3.23	0.955	0.7	0.20	2.58	0.694
Deprivation					0.9	0.85	1.03	0.153	1.0	0.86	1.05	0.699
Antenatal Anxiety												
No									-			
Yes									2.9	3.16	11.34	0.003
Antenatal Somatising												
No									-			
Yes									2.0	1.36	4.07	0.024

Appendix J:
Table 13.1 Stringent Multivariable Model 4.1

Table 13.1. Stringent multivariable logistic regression Model 4.1 for types of life events during mid-pregnancy to the early postnatal period and postnatal depression symptoms (depressed; *N* = 87; not depressed; *N* = 820)

	Unadjusted (Model 1)				Antenatal Depression (Model 2)				Demographics (Model 3)				Antenatal Comorbidity (Model 4)			
	95% CI				95% CI				95% CI				95% CI			
Variable	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value	OR	Upper	Lower	*p* value
Social/friendship problem																
No	-				-				-				-			
Yes	3.1	1.27	7.84	0.014	3.6	1.37	9.46	0.009	3.4	1.25	9.00	0.016	3.7	1.35	10.00	0.011
Financial crisis																
No	-				-				-				-			
Yes	2.6	0.79	8.68	0.114	3.1	0.87	10.67	0.081	2.8	0.80	10.01	0.105	1.8	0.45	6.84	0.419
Antenatal Depression																
No					-				-				-			
Yes					11.1	6.33	19.47	0.00	10.9	6.16	19.40	0.00	2.7	1.31	5.67	0.008
Age (years)																
<20									3.9	0.96	16.26	0.057	3.1	0.66	14.62	0.153
21-30									1.1	0.68	1.89	0.626	1.0	0.61	1.79	0.874
31-40																
41-50									1.0	0.29	3.23	0.955	0.7	0.20	2.58	0.616
Deprivation									0.9	0.85	1.03	0.153	0.9	0.86	1.05	0.276
Antenatal Anxiety																
No									-				-			
Yes													6.0	3.16	11.34	0.000
Antenatal Somatising																
No									-				-			
Yes													2.4	1.36	4.07	0.002