



## Review article

# The presence of anxiety, depression and stress in women and their partners during pregnancies following perinatal loss: A meta-analysis



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## ABSTRACT

**Background:** Research indicates perinatal loss is associated with anxiety, depression and stress in women and partners during subsequent pregnancies. However, there are no robust estimates of anxiety, depression and stress for this group. We meta-analytically estimated rates of anxiety, depression and stress in pregnant women and their partners during pregnancies after previous perinatal loss.

**Methods:** Databases (Medline, PsychInfo, Embase, Cinahl Plus) and grey literature were searched from 1995 through to May 2016. Search terms included: depression, anxiety, or stress with perinatal loss (miscarry\*, perinatal death, spontaneous abortion, fetal death, stillbirth, intrauterine death, TOPFA) and subsequent pregnancy. Case-controlled, English-language studies using validated measures of anxiety, depression or stress in women or partners during pregnancy following perinatal loss were included. Data for effect sizes, study and demographic data were extracted.

**Results:** We identified nineteen studies representing  $n = 5114$  women with previous loss;  $n = 30,272$  controls;  $n = 106$  partners with previous perinatal loss; and  $n = 91$  control men. Random effects modelling demonstrated significant effects of perinatal loss on anxiety ( $d = 0.69$ , 95% CI = 0.41–0.97) and depression ( $d = 0.22$ , 95% CI = 0.15–0.30) in women; but no effect on stress ( $d = -0.002$ , 95% CI = -0.0639 to 0.0605).

**Limitations:** This study was limited by the quality of available studies, underpowered moderator analyses and an inability to examine additional covariates. Insufficient data were available to generate reliable effects for psychological distress in partners.

**Conclusions:** Our findings confirm elevated anxiety and depression levels during pregnancies following perinatal loss. Further research on predictors of distress in women and their partners is required.

## 1. Introduction

Each year in the UK, many women and their partners experience a perinatal loss (Manktelow et al., 2016; NISRA, 2016; NRS, 2016; ONS, 2016). Perinatal loss includes miscarriage (fetal death before 24 weeks' gestation), termination of pregnancy for fetal anomaly (TOPFA), stillbirth (when a baby is born dead after 24 weeks' gestation) and neonatal death. The majority of these women and their partners experience another pregnancy after their perinatal loss (Redshaw, 2014). Consequently, it is important to consider how perinatal loss may affect the well-being of these individuals and their babies during pregnancies subsequent to these losses.

Several studies (Armstrong, 2004; Bergner et al., 2008; Hughes et al., 1999; Robertson Blackmore et al., 2011) and a systematic review (Debackere et al., 2008) have reported an association between perinatal loss and anxiety, depression and stress in women during subsequent pregnancies. However, reliable estimates are hampered by considerable

methodological variability in the literature due to small sample sizes (Armstrong, 2004; Gaudet, 2010; Hughes et al., 1999), self-selecting research participants (Armstrong and Huttu, 1998; Armstrong, 2002; Huttu et al., 2011), self-report measures (Bergner et al., 2008; Debackere et al., 2008; Robertson Blackmore et al., 2011) and variation across studies in terms of perinatal loss definitions, types of losses and types of anxiety measured.

That notwithstanding, research into support during pregnancies following perinatal loss has been prioritised by the James Lind Alliance (JLA, 2015). This is further underlined by the potential immediate and long-term implications of psychological distress after perinatal loss, including continued anxiety, depression and stress postpartum and lower parental attachment to their baby during pregnancies following perinatal loss (Armstrong and Huttu, 1998; Gaudet, 2010). Pregnancy-specific anxiety, depression, PTSD and grief intensity during pregnancies following perinatal loss have also been linked to poorer intimate partner relationships (Huttu et al., 2015).

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Studies of women without previous perinatal loss experiences can be extrapolated to suggest that anxiety, depression and stress during subsequent pregnancies may also be associated with higher risks of pre-term birth, lower birth weight and poor infant development (Ding et al., 2014; Dunkel Schetter and Tanner, 2012; Graignic-Philippe et al., 2014; Grigoriadis, 2013; Mulder et al., 2002). However, one study found that children born following stillbirth were not at risk of experiencing cognitive or health problems at 6–8 years of age (Turton et al., 2009a).

Although there has been a systematic review of this literature (Debackere et al., 2008), this included non-validated measures of anxiety, depression and stress; and did not quantify rates of common mental health difficulties.

Therefore, the current meta-analysis sought to generate effect sizes for the presence of anxiety, depression and stress for women and their partners in relation to control groups; and to model potential moderators of these effects. We hypothesized that anxiety, depression and stress would be significantly higher in women and their partners during pregnancy following perinatal loss than in controls.

## 2. Methods

### 2.1. Search criteria

This meta-analysis was conducted following MOOSE (Stroup et al., 2000) and PRISMA guidelines (BMJ, 2009). A comprehensive search was conducted using Ovid (Medline, PsychInfo and Embase) and EBS-COhost (Cinahl Plus) databases for research published between 1995 and May 2016. This search included studies published in the last 20 years when improved bereavement care following perinatal loss has been increasingly emphasised in many regions. A ‘grey literature’ search was performed using Open Grey, Virtual Health Library and Grey Literature Report. Reference lists of all included studies were checked. The search strategy used combinations of the following search terms: anxiety OR depression OR stress AND perinatal loss, perinatal death, miscarriage, spontaneous abortion, stillbirth, neonatal death and termination of pregnancy for fetal anomaly AND subsequent pregnancy (see Appendix S1). The search was developed in consultation with a specialist librarian

### 2.2. Eligibility criteria

Quantitative observational studies were included according to the following criteria: included women and/or their partners during pregnancy following perinatal loss (including miscarriage, stillbirth, TOPFA and/or neonatal death); had a control group with pregnant women and/or their partners with no previous perinatal loss experience; used at least one validated anxiety disorder, depression or stress diagnostic tool; and published in English. No inclusion limits were imposed based on whether women and/or their partners have other children or the time elapsed between perinatal loss experience and subsequent pregnancy.

### 2.3. Search results

Two researchers (AH, LT) independently assessed all non-duplicate search for inclusion using Microsoft Excel 2010 and Endnote X7. Titles and abstracts were screened. Full-text manuscripts were assessed and reasons for exclusion or inclusion were recorded. When multiple records presented data for the same cohort, the record with the most comprehensive results was included. The authors of five studies were contacted as insufficient data were published. Where study inclusion could not be agreed the third researcher (AM) was consulted and a consensus agreement reached.

### 2.4. Data extraction

Relevant data from included studies were extracted using Microsoft Excel. Data were extracted for study country, year, perinatal losses included, timing of assessment, psychological distress results and diagnostic tools used (see Appendix S2 for full details).

### 2.5. Quality assessment

Adapted versions of the Agency for Healthcare Research and Quality (AHRQ) checklist and related guidance notes were used by two independent researchers (AH, LT) to assess the quality of each study included (Williams et al., 2010) (see Appendices S3 and S4). Criterion 8 was excluded from the final scoring of the AHRQ checklists as longitudinal data were not analysed.

Independent quality assessments were compared and consensus scores reached for the purposes of the meta-analysis.

### 2.6. Analysis plan

Analyses were completed using R Studio (V0.99.489). Independent group studies that reported mean scores and standard deviations for anxiety, depression or stress, effect sizes were calculated as Cohen's *d*. Odds ratios (ORs) were used where mean score and standard deviation data were unavailable. Where ORs were unreported but the numbers of participants with anxiety or depression were available, ORs and confidence intervals were calculated (Szumilas, 2010). All ORs were converted into standardised Cohen's *d* values and the standard errors of these effect sizes were calculated using the methods indicated by Borenstein et al. (2009) and Chinn (2000).

A random-effects model was used to weight studies and calculate a summary effect size as differences in sample sizes and covariates (e.g. different perinatal loss types or demographic characteristics) may create variations in effect sizes across studies (Borenstein et al., 2009). DerSimonian-Laird's method was used to calculate summary effects using fixed and random effects modelling with R packages ‘meta’ (Schwarzer, 2016), ‘metafor’ (Viechtbauer, 2010) and ‘metagen’ (Möbius, 2014). Confidence intervals of 95% and standard errors for each effect size were also calculated. Z-values and *p* values were computed to test the null hypotheses for each analysis. The *Q* and *I*<sup>2</sup> statistics were used to analyse heterogeneity and quantify observed variance. Influence analyses, publication bias and outlier biases were analysed using funnel plots and the Duval and Tweedie (2000) “trim and fill” method (Varese et al., 2012).

As most of the available data focused on women, the main analyses examined anxiety, depression and stress in women during subsequent pregnancies. Moderator analyses were conducted to determine whether the type of perinatal loss experienced, trimester when women were assessed for these conditions and country of study affected the results of the main analyses. Meta-regression was used to determine whether predictors of these conditions included the year of the study (based on the assumption that bereavement care following perinatal loss has improved in the last 20 years in countries such as the UK) or quality rating of the study (assuming results were influenced by study quality). Separate random effects modelling was also used to examine the effect of perinatal loss on pregnancy-specific and trait anxiety. Secondary analyses of anxiety and depression-specific data for men during pregnancies subsequent to perinatal loss were also performed.

### 2.7. Project registration

The details of this study were registered on Prospero (CRD42016037951).

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