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The mental health impact of perinatal loss: A systematic review and meta-analysis

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ABSTRACT

Perinatal loss can pose a significant risk to maternal mental health. There is limited data on the strength of association between perinatal loss and subsequent common mental health disorders (CMHD) such as anxiety, depression and post-traumatic symptoms (PTS). A systematic review and meta-analysis identified studies with control groups, published between January 1995 and March 2020 reporting validated mental health outcomes following perinatal loss. We identified 29 studies from 17 countries, representing a perinatal loss sample (n = 31,072) and a control group of women not experiencing loss (n = 1,261,517). We compared the likelihood of increased CMHD in both groups. Random-effects modelling on suggested that compared to controls, perinatal loss was associated with increased risk of depressive (RR = 2.14, 95% CI = 1.73–2.66, $p < 0.001$, $k = 22$) and anxiety disorders (RR = 1.75, 95% CI = 1.27–2.42, $p < 0.001$, $k = 9$). Compared to controls, Perinatal loss was also associated with increased depression (SMD = 0.34, 95% CI = 0.20–0.48, $p < 0.001$, $k = 12$) and anxiety scores (SMD = 0.35, 95% CI = 0.12–0.58, $p < 0.003$, $k = 10$). There were no significant effects for post-traumatic stress (PTS) outcomes ($k = 3$). Our findings confirm that anxiety and depression levels following perinatal loss are significantly elevated compared to "no loss" controls (live-births, non pregnant from community, or difficult live births). Elevated depression and anxiety rates were also reported for those who experienced loss during later stages of pregnancy. Assessing mental health following loss is a maternal health priority.

1. Introduction

Perinatal loss is a prevalent health concern with one in four pregnancies ending in loss (Armstong, 2004; Christiansen, 2017). Around 2.6 million stillbirths are reported globally each year (Lancet, 2016) and 14–20% of all pregnancies are reported to end in miscarriage (Farquharson et al., 2005). Miscarriage (foetal loss prior to 20–28 weeks), stillbirth (foetal loss following 20–28 weeks), neonatal death (loss occurring within the first 28 days of life), termination of pregnancy due to foetal anomaly (TOPFA) and recurrent perinatal loss (RPL; two or more experiences of loss) all fall under the umbrella term of perinatal loss. For many women, the trauma of perinatal loss at any stage can have a significant effect on their well-being, and for some expectant mothers, the emotional toll is sufficiently severe to lead to a diagnosis of psychiatric disorder.

There is increasing evidence for associations between perinatal loss and common mental disorders including: depression, anxiety, and post-traumatic stress (PTS); all of which can develop in addition to the natural process of grieving (Adib-Rab et al., 2019; Gravensteen et al., 2012; Price and McLeod, 2012; Brier, 2004); although the association between PTS and perinatal loss has only more recently been investigated (Isguder et al., 2017). While studies have shown there to be strong association with anxiety, depression, and PTS globally, the prevalence rates and risk factors are not fully understood (Daugirdaitė et al., 2015; Farren et al., 2018). Review and meta-analytic data suggest evidence for associations between perinatal loss and psychological reactions following miscarriage (Adolfsson, 2011); with 8–20% of women showing symptoms for moderate depression, 18–32% for anxiety at four to six weeks following loss; and rates of between 25 and 39% for post-traumatic stress disorder (PTSD) at one month following loss (Farren et al., 2018).

Systematic reviews and meta-analyses have identified evidence for associations between perinatal loss and psychological reactions following miscarriage (Adolfsson, 2011); experience of grief and stigma after stillbirth (Burden et al., 2016); mental health risk after early pregnancy loss (Farren et al., 2018); and the presence of common mental

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disorders presenting in subsequent pregnancies following perinatal loss (Hunter et al., 2017); However, there is limited meta-analytic evidence for estimates of anxiety, depression and PTS rates for women following loss; and correlates of any association (Quenby et al., 2021).

Furthermore, health care system differences and inequalities of access to maternal care further complicate efforts to identify those at greatest risk. Although 98% of stillbirths occur in low and middle-income (LMI) countries ((Lawn et al., 2016), 90% of perinatal loss research is conducted within high-income countries (Farren et al., 2018). The high incidence of loss within low and middle-income settings and lack of research highlights the need for an analysis of global prevalence rates and identification of risk factors for mental health outcomes following perinatal loss.

Methodological inconsistencies between studies present a further barrier to establishing a robust picture of the size and scale of the mental health aspect of loss. For instance, how loss is categorised, when mental health outcomes are measured, and the composition of comparison samples can all significantly influence reported results. Consideration of an appropriate control group is especially important within this body of research to understand potential variability in estimates. However, the pregnancy status of the control group (such as pregnant or not, or in some studies use of a 'difficult live birth' control) or baseline mental health difficulty levels in the population may reduce baseline differences between the study group and the control (Dennis et al., 2017). The impact of maternal age and quality of studies, including the measurement of mental health outcome are also of importance. From a policy and practice perspective, accurate estimates of the mental health impacts of perinatal loss and it's correlates can inform service planning, quantify risk, and identify those most at risk. This in turn can enable needs-matched interventions that are appropriate and acceptable to women and their support networks (Quenby et al., 2021).

To our knowledge there has not been a comprehensive meta-analysis estimating rates of anxiety, depression and PTS for women following perinatal loss (from conception through to 28 days post-delivery). In the current study we aimed to synthesise data reporting the effects of perinatal loss on common mental health outcomes, namely anxiety, depression, and post-traumatic stress; and to identify potential moderators of these associations, including study quality, type of loss, trimester of loss, income status of study country and maternal age. We hypothesised that outcome measures of depression, anxiety and PTS will be significantly elevated following perinatal loss in comparison to controls.

2. Methods

2.1. Search strategy

A broad search strategy was developed with the guidance of a health librarian, adhering to MOOSE guidelines for observational studies (Stroup et al., 2000) and the PRISMA checklist for systematic reviews and meta-analyses (Page et al., 2021). A comprehensive electronic database search was performed using the following databases: EBSCO (CINAHL Plus), Ovid (Embase, PsycINFO, MEDLINE, Global Health) and Web of Science, identifying studies and reviews published between 1 January 1995 and 2 March 2020. Following Hunter et al. (2017), we set 1995 as the lower limit to reflect a timeframe in which greater uniformity in the reporting standards of clinical data around perinatal loss has emerged.

The search strategy applied to the cited databases included alternative spellings for common mental health terms (anxiety, depression, PTS) and perinatal loss terms (miscarriage, stillbirth, TOPFA, neonatal death) combined with Boolean operators (see Appendix S1). Open Grey, the Virtual Health Library and the Grey Literature Report were searched for 'grey literature' along with the WHO International Clinical Trials Registry Platform (ICTRP) and the Cochrane Central Register of Controlled Trials (CENTRAL). A hand search and snowball sampling of the selected study reference lists was performed for additional unpublished studies missed by the electronic search or not captured in the initial scoping review.

2.2. Eligibility criteria

Quantitative observational studies included within this meta-analysis met the following criteria: sampled women who had experienced perinatal loss (miscarriage, stillbirth, TOPFA or neonatal death); studies where all participants were assessed for anxiety, depression and/or PTS with at least one validated self-report measure or clinical diagnostic tool; studies published in English; studies contained a control group of women with no experience of perinatal loss including pregnant women, those who had a successful pregnancy, those attempting pregnancy and those who were not pregnant from the community.

Studies were excluded if i) participants included women who experienced the loss of an infant after 28 days post-delivery or women who elected to have an abortion unrelated to foetal anomalies or a maternal medical condition. Ii) Studies of fathers only were excluded at the record stage, while parent and couple studies were retained and screened. Studies that explored a iii) specialised aspect of either maternal health (e.g. twin studies); iv) medical health (e.g. substance abuse) or v) psychological and social health (e.g. intimate partner violence) were also excluded. Finally, vi) studies containing populations living in extreme conditions (e.g. Ebola outbreak) were also excluded. Full exclusion criteria are listed in Appendix S2.

2.3. Search results

After duplicates were removed electronically through Ovid, all records were collected into Endnote X9, electronically scanned again for duplicates and exported into a Microsoft Excel table. Titles and abstracts were screened once by a researcher. Records that did not pertain to mental health outcomes following perinatal loss were excluded. The remaining full-text articles were then systematically screened blind by two independent researchers who applied the predefined criteria and recorded reasons for exclusion in the table. Where multiple records reported data from the same study cohort, the most comprehensive study was retained for analysis. The final results were compared, and discrepancies were resolved via a consensus discussion with the other members of the research team.

2.4. Data extraction

Aggregate study characteristics and population data were extracted from the remaining studies and recorded blind by two independent researchers using a Microsoft Excel table. Participant obstetric details, demographic data and country income group were recorded where provided. The type of loss and corresponding gestation period for the sample and the pregnancy status of the control group, where applicable, were noted. Mental health outcomes (anxiety, depression and/or PTS) were recorded along with the diagnostic tool(s), associated cut-off scores and specified time periods between loss and the mental health assessment. Raw data (sample size, mean scores, standard deviation and/or count data) to calculate study effect sizes for mental health outcomes of both the perinatal loss and control groups was extracted. Studies were excluded where baseline data was unavailable. (see Appendix S3 for summary data)

2.5. Quality assessment

An adapted Agency for Healthcare Research and Quality (AHRQ) methodological checklist and the corresponding guidance notes were modified and applied to the individual studies to assess risk of bias (Williams et al., 2010) (see Appendix S3 and S4). This assessment tool allowed researchers to gauge the internal validity, applicability and

completeness of reporting for the selected studies. A numeric value was allocated to the grading scale of an 11 criteria checklist. Criterion #8 was only applicable to studies with a longitudinal design. A maximum score of 22 for longitudinal studies and 20 for non-longitudinal studies could be achieved, with all ratings converted to a percentage score. The quality assessment was completed by two independent researchers and any discrepancies between the scores were resolved through discussion and further reference to the guidance notes.

2.6. Analysis plan

Statistical analyses were performed with RStudio 3.6.2. Effect sizes for each study were calculated, weighted and combined into a summary effect size for each outcome (depression, anxiety and PTS) using random effects modelling (Borenstein et al., 2009). Pooled results were analysed yielding effect estimates, confidence intervals (CI's) and significance values. The inverse variance method and DerSimionian-Laird estimator (DerSimonian, 1986) were used with R packages 'meta' (Schwarzer, 2016) and 'metafor' (Viechtbauer, 2010) to calculate the summary effects and perform the meta-analyses.

For categorical data, where only the sample size and outcome count data were available, the effect size was calculated as a risk ratio (RR) with a 95% confidence interval. For studies that reported continuous data through a mean score and standard deviation (SD) for anxiety, depression and PTS outcomes, effect sizes were calculated as a standardised mean difference (SMD) with a 95% confidence interval. The Z values and p values were computed to test the null hypotheses for each outcome and the Cochran Q test and I^2 statistic (Higgins et al., 2019) were calculated to test for heterogeneity and to quantify the observed variance.

Influence analysis was applied to identify sources of heterogeneity and to quantify between-study variance. The Duval and Tweedie (2000) 'trim-and-fill' method was used to test publication bias, allowing for analysis of the results with the exclusion of outliers and inclusion of possible missing studies.

Moderator analyses of subgroups were also performed to assess whether the type of loss group, control group and country ranking affected the outcome of the main analyses and could account for the level of heterogeneity. Between variable analyses and separate random-effects modelling of sub-groups were also performed. Meta-regression statistical models were used to further assess if the quality of each study or the age of the participants affected outcomes (Borenstein et al., 2009). Sub-analyses were dependant on the number of studies and data available for each variable after separating categorical from continuous data.

2.7. Project registration

A study protocol was registered with Prospero on 24/06/2020 (CRD42020172829).

3. Results

3.1. Study selection and characteristics

The initial search produced 8638 published records with no additional studies found through the 'grey literature' and reference list search. Once duplicate records were removed electronically and titles/abstracts screened by the authors, the remaining 793 full-text articles were systematically reviewed against the pre-defined inclusion criteria. Records excluded at this stage were duplicates, father and couple studies and studies conducted with samples from specific populations, such as women with high-risk medical conditions or those living in extreme environmental conditions. Of the remaining articles assessed for eligibility, 32 studies were excluded due to the absence of observed control group, 20 studies contained duplicate cohort data and 5 studies lacked sufficient data for our analysis (Fig. 1). No authors were contacted for further information as there was sufficient data available in the final group of published studies to perform the intended analyses.

Study characteristics and participant details of the 29 included papers are detailed in Appendix S3. Total participant size was N = 1292,589 (perinatal loss sample n = 31,072, control group n = 1261,517), with an age range of 13–57 years. One study had a comparatively large sample (loss group n = 8292, control n = 1194,758; Lewkowitz et al., 2019), while the remaining 28 studies contained a total of 89,539 participants (sample n = 22,780, control n = 66,759). Only one study had less than 100 women in the total sample (n = 65; Ng et al., 2017). One study contained datasets from two independent population studies (Toffol et al., 2013).

Miscarriage accounted for most of the reported loss type in the studies (n = 14,516), followed by stillbirth (n = 8715), recurrent loss (n = 1188) and TOPFA (n = 62). The remaining studies reported grouped loss (n = 6591), with some reporting stillbirth and neonatal death combined (n = 5095) and others reporting perinatal loss undifferentiated by type (n = 1496). The control groups contained either participants with live births (n = 1257,048), non-pregnant participants from the community (n = 4062), participants who were pregnant (n = 339) or had a difficult pregnancy (n = 67). Of the 29 studies, all reported data for depression outcomes, 16 (55%) reported anxiety outcomes and 3 (10%) reported PTS outcomes. Categorical data was reported in 21 studies (72%), continuous data reported in 15(52%) and 7 (24%) contained outcome data for both.

Only four studies recruited participants between 1985 and 2000 while 25 assessed participants between 2000 and 2019, of which 21were from 2010 to 2019. Studies reported data from 17 different countries and one study recruited participants online from a group of high-income countries (USA, UK, Europe, Canada, Australia, New Zealand). A total of 16 studies (55%) took place in high-income countries (UK, US, Australia, Denmark, Finland, Norway, Germany) assessing 1241,617 participants (96%) and 13 (45%) were conducted in low and middle-income (LMI) countries with 50,972 participants assessed (4%), of which 7 (24%) were classified as middle-income (Turkey, Malaysia, Iran, Sri Lanka, China) and 6 (21%) as low-income (Bangladesh, India, Nigeria, Benin, Burkina Faso).

3.2. Depression following perinatal loss

Of the 29 studies that assessed clinically diagnosed or significant depression, 21 studies (22 datasets) were assessed in the categorical group and 12 studies in the continuous group. Random effects modelling for categorical depression outcomes (presence or absence of depression) resulted in a significant medium size effect for the association between perinatal loss and depression (RR = 2.14, 95% CI = 1.73–2.65, Z = 6.94, $p < 0.001$, k = 22; Fig. 2)Figure 2. Influence analysis identified one study as a potential outlier (Toffol et al., 2013). Exclusion of this study slightly increased the effect size (RR = 2.31, 95% CI = 1.86–2.87, Z = 7.61, $p < 0.001$, k = 20). Random effects modelling of continuous depression outcomes (mean depression score) suggested a medium size significant association (SMD = 0.34, 95% CI = 0.20–0.48, Z = 4.62, $p < 0.001$, k = 12; Fig. 3). Omitting a possible outlier (Budak et al., 2016) had a negligible impact on the effect estimate (SMD = 0.37, 95% CI = 0.24–0.51, Z = 5.39, $p < 0.001$, k = 11).

Heterogeneity was substantial and significant for categorical outcomes (Q = 257.93, $p < 0.001$, I^2 = 91.9%), but with no evidence of publication bias (Eggers' test, p = 0.39). 'Trim and fill' analyses identified six hypothetical missing studies but modelling these suggested a significant effect of perinatal loss on depression would remain (RR = 1.76, 95% CI = 1.40–2.21, Z = 4.87, $p < 0.001$, k = 28). Heterogeneity and publication bias was similar for continuous outcomes, and no missing studies were identified using 'trim and fill'. (Q = 42.17, $p < 0.01$, I2 = 76.3%; 95% CI = 57.5%–86.8%; Egger's test p = 0.30.

Moderator analysis of categorical outcomes indicated no significant

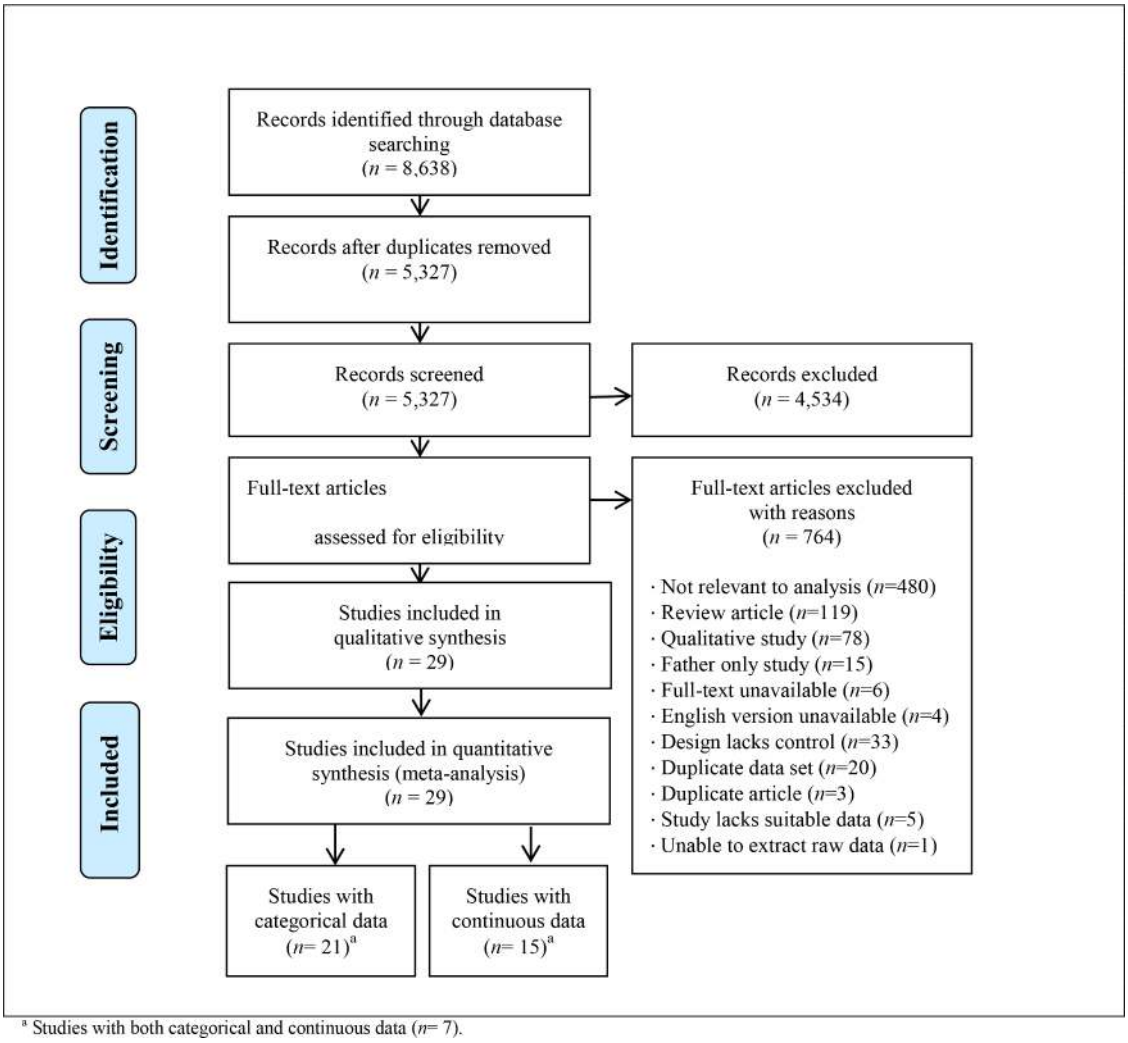

Fig. 1. PRISMA flow diagram detailing study selection process. [a] Studies with both categorical and continuous data ($n = 7$).

effect of different types of loss on effect size magnitude ($p = 0.16$), although effect size for late loss were larger than those for early loss (Table 1). Recurrent loss had the largest effect on depression, followed by neonatal death, stillbirth, miscarriage, TOPFA and grouped loss (Table 1). Analysis of control group types, or income level of country did not show significant differences ($p = 0.77$; and $p = 0.63$; Table 1).

Moderator analysis of continuous outcomes, indicted a significant difference for type of loss ($p < 0.001$) with late loss leading to larger effect sizes for depression than early loss (Table 1.) TOPFA had the largest magnitude effect, followed by stillbirth, recurrent loss and grouped loss. Analysis of control group type showed a significant effect ($p < 0.001$) with live birth controls leading to a larger effect size for depression in the loss group, compared to community and pregnant controls (Table 1). Rates of depression were higher in controls with a difficult birth group than for women who had experienced loss. Country level of income was not associated with group differences ($p = 0.82$; Table 1). Meta-regression analysis indicated that age did not have a significant effect on depression levels for either categorical ($\beta = -0.0059$, SE = 0.008, $p = 0.56$) or continuous outcomes ($\beta = 0.007$, SE = 0.77, $p = 0.89$).

3.3. Anxiety following perinatal loss

Of the 16 studies that assessed diagnosed, or significant anxiety, 9 studies contained categorical measures (presence/absence of anxiety) and 10 reported continuous outcomes (anxiety score). Random effects modelling of categorical outcomes suggested a small but significant effect of perinatal loss on increased levels of anxiety compared to controls (RR = 1.75, 95% CI = 1.27–2.42, $Z = 3.44$, $p < 0.001$, $k = 9$; Fig. 4). Influence analysis identified one study as a potential outlier (Toffol et al., 2013). Exclusion of this study slightly increased the summary effect estimate (RR = 1.91, 95% CI = 1.37–2.67, $Z = 3.79$, $p < 0.001$, $k = 8$). Random effect modelling of continuous outcomes also suggested a moderate but significant association (SMD = 0.35, 95% CI = 0.12–0.58, $Z = 3.04$, $p = 0.003$, $k = 10$; Fig. 5). After omitting a possible outlier (Budak et al., 2016), analysis suggested a slightly, larger effect on a narrower confidence interval (SMD = 0.39, 95% CI = 0.29–0.49, $Z = 4.03$, $p < 0.001$, $k = 9$).

Analysis suggested high heterogeneity for categorical outcomes ($Q = 55.86$, $p < 0.001$, $I^2 = 85.7\%$), but no significant publication bias (Eggers' test; $p = 0.73$). 'Trim and fill' analyses identified two hypothetically missing studies. Re-running the analysis with these studies modelled a reduced yet still significant effect of perinatal loss on increased levels of anxiety (RR = 1.57, 95% CI = 1.14–2.16, $Z = 2.77$, $p = 0.006$, $k = 11$). The heterogeneity pattern and publication bias was mirrored for continuous outcomes ($Q = 46.55$, $p < 0.001$, I2 = 80.7%; Egger's test; $p = 0.79$). No additional studies were identified as missing from the analysis using the "trim and fill" method.

A sub-analysis for the effect of different loss groups showed a significant effect on categorical anxiety outcomes ($p < 0.001$), with the late

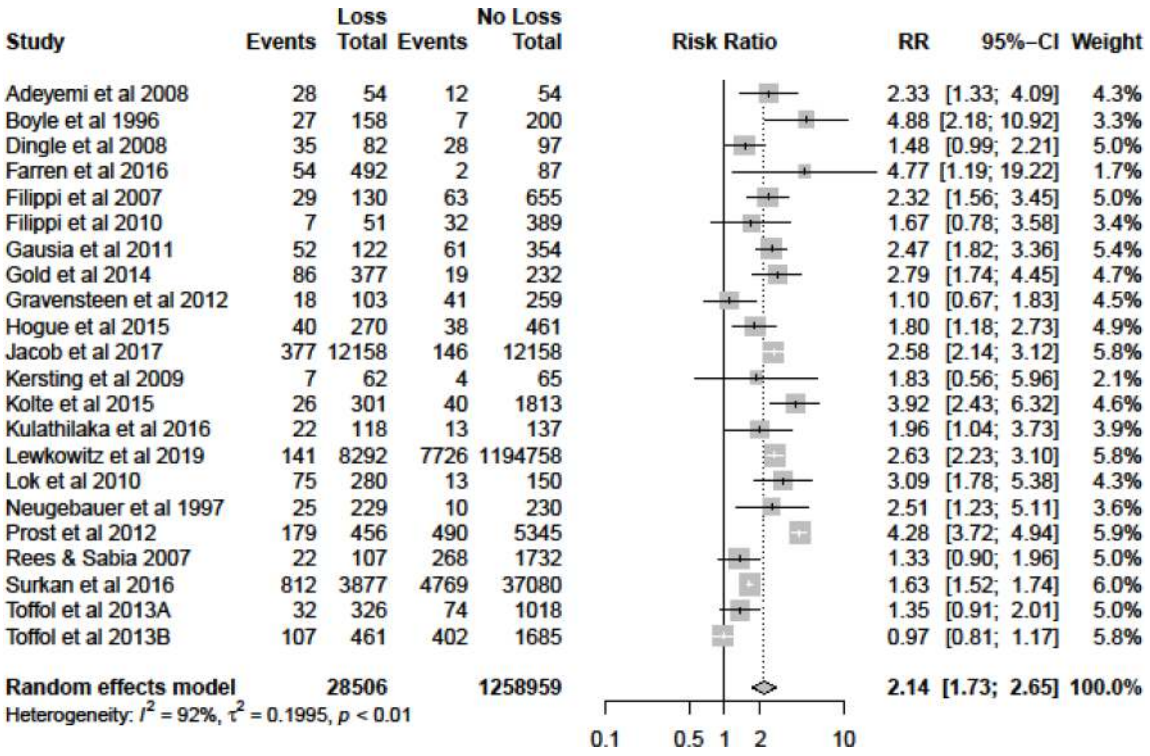

Fig. 2. Forest plot of effect sizes for categorical depression outcomes in women following perinatal loss. *Note*. RR = Risk ratio; CI = Confidence interval.

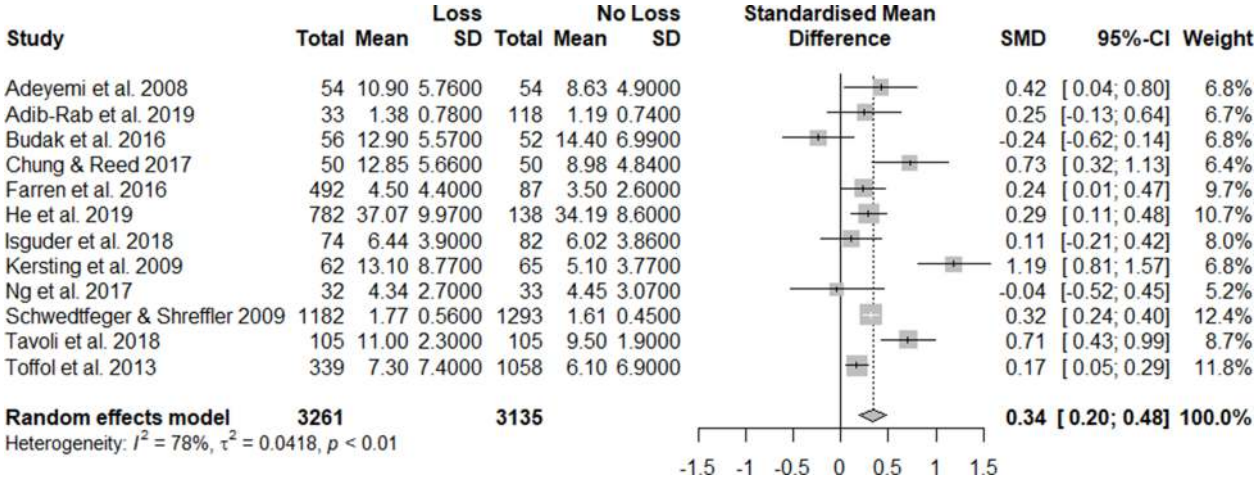

Fig. 3. Forest plot of effect sizes for continuous depression scores following perinatal loss. *Note.* SMD = Standardised mean difference; CI = Confidence interval; SD = Standard deviation.

loss group showing a larger effect than the early loss group (Table 2). Neonatal death showed the largest effect of loss on increased rates of anxiety, followed by TOPFA, stillbirth and miscarriage (Table 2). Analyses of methodological differences in control groups and country income did not show significant group differences ($p = 0.80$ and $p = 0.82$ respectively; Table 2).

Moderator analysis also identified a significant effect of type of perinatal loss on continuous anxiety outcomes ($p = 0.001$), with a larger effect for late loss than early loss (Table 2). A further large effect was identified for TOPFA and a moderate effect for stillbirth. There was a significant effect of control group type of estimates ($p < 0.001$) with higher rates of anxiety found for the loss group when compared to live birth controls (Table 2). Higher levels of anxiety were also found within control groups who experienced difficult birth. No statistical significance was evident for country income ranking ($p = 0.14$; Table 2). Meta-regression suggested younger age had a small but significant effect on increased anxiety levels following perinatal loss for categorical ($\beta = -0.02$, SE = 0.01, $p = 0.01$) but not continuous outcomes ($\beta = -1.54$, SE = 1.90, $p = 0.41$).

3.4. *Post-traumatic stress following perinatal loss*

Only three studies reported PTS outcomes for both sample and control groups; all using continuous outcomes. Random effects modelling showed a non-significant effect for the association between perinatal loss and elevated PTS outcomes (SMD = 0.66, 95% CI = -0.93–2.25, $Z = 0.81$, $p = 0.42$, $k = 3$). Between study heterogeneity was substantial (Q(d.f) = 113.97 (2), $p < 0.001$, $I^2 = 98.2\%$). Although there was no evidence of publication bias (Eggers' test; $p = 0.30$).

Table 1
Results of moderator analysis for depression following perinatal loss.

Moderator	Moderator group	Categorical outcomes				Continuous Outcomes			
		k	RR (95% CI), *p* value	*Q* test (df)	I^2 (%)	*k*	SMD (95% CI), *p* value	*Q* test (df)	I^2 (%)
Perinatal loss group	Group loss (MC, SB, NND)	2	1.75 (1.02–3.03), $p = 0.04$	3.86 (1)	74.1	2	0.07 (−0.47–0.61), $p = 0.79$	7.84(1)	87.3
	Early loss (MC)	9	1.90 (1.31–2.75), $p < 0.001$	62.48 (8)	87.2	7	0.27 (0.12–0.41), $p < 0.01$	14.33 (6)	58.1
	Late loss (SB, NND)	11	2.36 (1.73–3.22), $p < 0.0001$	173.43 (10)	94.2	1	0.42 (0.04–0.80), $p < 0.05$	–	–
	Stillbirth	5	1.97 (1.38–2.82), $p = 0.0002$	38.38 (4)	89.6	1	0.73 (0.32–1.13), $p < 0.05$	–	–
	Neonatal death	2	2.40 (0.99–5.85), $p = 0.05$	4.14 (1)	75.9	–	–	–	–
	TOPFA	1	1.83 (0.56–5.96), $p = 0.31$	0.00	–	1	1.19 (0.81–1.57), $p < 0.0001$	–	–
	RPL	1	3.92 (2.43–6.32), $p < 0.0001$	0.00	–	3	0.42 (0.14–0.70), $p < 0.05$	6.55 (2)	69.5
Control group	Live birth	17	1.95 (1.53–2.49), $p < 0.0001$	252.14 (16)	93.7	7	0.50 (0.30–0.70), $p < 0.001$	37.53 (6)	84.0
	Difficult birth	–	–	–	–	1	−0.24 (−0.62- 0.14), $p = 0.22$	–	–
	Pregnant	2	2.45 (1.16–5.19), $p = 0.02$	1.29 (1)	22.4	3	0.16 (−0.008- 0.34), $p = 0.06$	1.20 (2)	0.0
	Community Non-pregnant	4	2.72 (1.42–5.20), $p = 0.0025$	14.66 (3)	79.5	1	0.29 (0.11–0.48), $p < 0.05$	–	–
Country Ranking	High-income	14	2.03 (1.52–2.70), $p < 0.0001$	106.52 (13)	87.8	6	0.37 (0.15–0.59), $p < 0.05$	37.84 (5)	86.8
	Middle-income	2	2.54 (1.63–3.94), $p < 0.0001$	1.10 (1)	9.1	5	0.29 (0.06- 0.53), $p < 0.05$	11.47 (4)	65.1
	Low-income	6	2.36 (1.45–3.83), $p = 0.0005$	149.50 (5)	96.7	1	0.42 (0.04- 0.80), $p < 0.05$	–	–
	LMI	8	2.39 (1.58–3.61), $p < 0.0001$	152.03 (7)	95.4	6	0.32 (0.12–0.52), $p < 0.05$	11.71 (5)	57.3

Note. MC = Miscarriage; SB = Stillbirth; NND = Neonatal death; LMI = Low and middle-income countries.

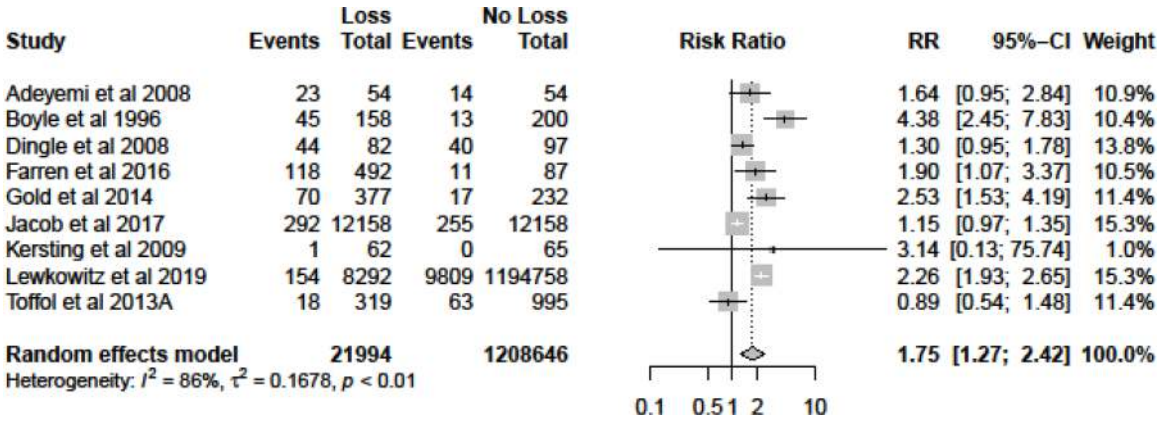

Fig. 4. Forest plot of effect sizes for categorical anxiety outcomes in women following perinatal loss. *Note.* RR = Risk ratio; CI = Confidence interval.

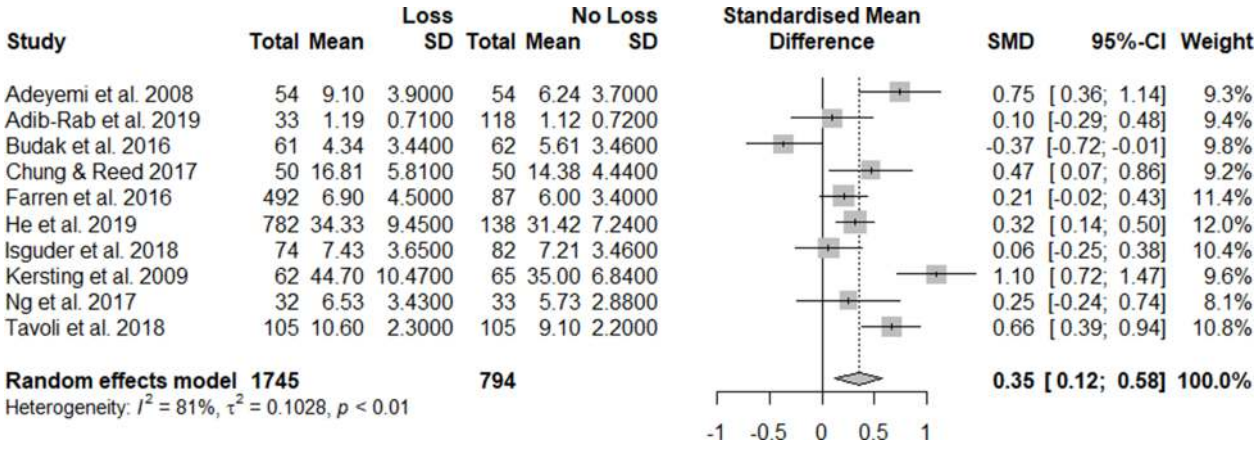

Fig. 5. Forest plot of effect sizes for continuous anxiety scores in women following perinatal loss. *Note.* SD = Standard deviation; SMD = Standardised mean difference; CI = Confidence interval.

3.5. Study quality

The final group of studies varied greatly in quality with AHRQ methodological scores ranging from 45/100 to 90/100 with a mean score of 71.5 (See Table 3). The recruitment strategy was clearly outlined in most papers. Five studies reported secondary population data (Lewkowitz et al., 2019; Schwerdtfeger and Shreffler, 2009; Toffol et al., 2013; Rees and Sabia, 2007; Jacob et al., 2017) while the remaining recruited participants through hospitals, clinics or government health records. In two instances the sample was recruited online (Budak et al., 2016) or through community groups (Chung and Reed, 2017). One study recruited only the second generation in a birth cohort (Dingle et al., 2008) and two obtained samples from the control arm of population randomised control trials (RCT; Prost et al., 2012; Surkan et al.,

Table 2
Results of moderator analysis for anxiety following perinatal loss.

Moderator	Moderator group	Categorical outcomes				*Continuous Outcomes*			
		k	RR (95% CI), *p* value	*Q* test (df)	I^2 (%)	*k*	SMD (95% CI), *p* value	*Q* test (df)	I^2 (%)
Perinatal loss group	Group loss (MC, SB, NND)	–	–	–	–	3	0.19 (−0.35–0.73), $p = 0.49$	17.15 (2)	88.3
	Early loss (MC)	4	1.21 (0.99–1.47), $p = 0.06$	4.30 (3)	30.2	6	0.28 (0.11–0.45), $p < 0.01$	10.57 (5)	52.7
	Late loss (SB, NND)	4	2.45 (1.81–3.31), $p < 0.0001$	6.35 (3)	52.8	2	0.61 (0.33–0.89), $p < 0.001$	0.97 (1)	0.00
	Stillbirth	2	2.91 (1.56–5.41), $p < 0.001$	3.82 (1)	73.8	1	0.47 (0.07–0.86), $p = 0.02$	0.00	–
	Neonatal death	1	4.42 (2.36–8.29), $p < 0.0001$	0.00	–	–	–	–	–
	TOPFA	1	3.14 (0.13–75.74), $p = 0.48$	0.00	–	1	1.09 (0.72–1.47), $p < 0.001$	0.00	–
	RPL	–	–	–	–	3	0.38 (0.09–0.66), $p < 0.01$	6.53 (2)	69.4
Control group	Live birth	8	1.74 (1.22–2.47), $p = 0.002$	55.61 (7)	87.4	6	0.45 (0.04–0.86), $p = 0.03$	39.25 (5)	87.3
	Difficult birth	–	–	–	–	1	−0.37 (−0.72-(−0.01)), $p = 0.04$	0.00	–
	Pregnant	1	1.90 (1.07–3.37), $p = 0.03$	0.00	–	3	0.17 (−0.00–0.34), $p = 0.06$	0.66 (2)	0.00
	Community Non-pregnant	–	–	–	–	1	0.32 (0.14–0.50), $p < 0.001$	0.00	–
Country Ranking	High-income	8	1.77 (1.25–2.51), $p = 0.001$	55.86 (7)	87.5	4	0.35 (−0.20–0.88), $p = 0.21$	32.1 (3)	90.7
	Middle-income	–	–	–	–	5	0.30 (0.08–0.51), $p < 0.01$	9.84 (4)	59.4
	Low-income	1	1.64 (0.95–2.84), $p = 0.08$	0.00	–	1	0.75 (0.36–1.14), $p < 0.001$	0.00	–
	LMI	–	–	–	–	6	0.36 (0.14–0.58), $p < 0.01$	14.02 (5)	64.3

Note. MC = Miscarriage; SB = Stillbirth; NND = Neonatal death; LMI = Low and middle-income countries.

2016). Most studies consisted of an unbiased selection of sample cohorts, with only a few studies providing little information on selection criteria (Adeyemi et al., 2008; Kersting et al., 2008), providing a vague description of recruitment strategy (Budak et al., 2016; Chung and Reed, 2017) or omitting a mental health assessment time point (Lok et al., 2010).

Most studies clearly defined a sample group by type of perinatal loss. Some studies created specified subgroups (Boyle et al., 1996; Farren et al., 2016; He et al., 2019; Surkan et al., 2016; Filippi et al., 2007), while others combined various types of loss into one group (Filippi et al., 2010; Prost et al., 2012; Rees and Sabia, 2007; Schwerdtfeger and Shreffler, 2009; Gold et al., 2014; Budak et al., 2016; Adeyemi et al., 2008). Most studies adequately recorded demographics for both the sample and control groups. While some provided overall demographics, others reported just the sample without the control (Lok et al., 2010) or provided minimal details for both groups (Tavoli et al., 2018; Jacob et al., 2017; Dingle et al., 2008; Farren et al., 2016). No studies conducted any form of blinding and this limitation was explicitly stated in three studies (Hogue et al., 2015; Filippi et al., 2010; Lewkowitz et al., 2019).

The sample size was justified with a power analysis in some studies (Chung and Reed, 2017; Tavoli et al., 2018; Farren et al., 2016; Kulathilaka et al., 2016; Gravensteen et al., 2012; Isguder et al., 2018; Filippi et al., 2007), whilst others obtained a large sample from population studies and may have considered power issues (Lewkowitz et al., 2019; Prost et al., 2012; Surkan et al., 2016; Jacob et al., 2017). Of the studies that reported response rates, the number of women who declined to respond or participate ranged from 5.9% (He et al., 2019) to 68.5% (Gravensteen et al., 2012). Some studies reported an attrition rate <10% (Prost et al., 2012; Rees and Sabia, 2007; Filippi et al., 2007) while two studies reported an attrition rate over multiple time points >50% (Farren et al., 2016; Hogue et al., 2015). Overall, the missing data reported by the studies was <20%.

While most studies performed appropriate analyses and provided multiple comparisons taking into consideration factors that influence differences, five studies were less robust than most in their analysis (Adeyemi et al., 2008; Budak et al., 2016; Ng et al., 2017; Schwerdtfeger and Shreffler, 2009; Tavoli et al., 2018) and four studies only minimally controlled for possible confounding variables (Jacob et al., 2017; Kulathilaka et al., 2016; Schwerdtfeger and Shreffler, 2009; Tavoli et al., 2018).

Meta-regression analyses for studies with categorical data revealed quality ranking scores had a small but significant effect on elevated anxiety outcomes ($\beta = 0.04$, SE = 0.01, $p = 0.01$) yet it did not significantly impact on depression outcomes ($\beta = 0.0034$, SE = 0.02, $p = 0.83$). Conversely, for studies with continuous data meta-regression suggested that study quality had a significant effect on elevated depression outcomes ($\beta = 0.32$, SE = 0.04, $p < 0.001$) but did not influence anxiety effect sizes ($\beta = 0.0026$, SE = 0.015, $p = 0.86$).

4. Discussion

4.1. Main findings

The results of this meta-analysis are consistent with previous research (Farren et al., 2018) and support the hypothesis that perinatal loss experienced by women impacts on subsequent mental health outcomes. The studies contained within the review were not restricted by geographic region, and all mental health outcomes were derived from validated measures. The association between perinatal loss and elevated levels of anxiety and depression is consistent across loss types, comparison groups and country income rankings. A non-significant effect for loss and PTS outcomes was identified from a small, heterogenous sample of studies. These findings underscore the global importance of understanding the sequelae of miscarriage and perinatal loss, highlighting the relative lack of evidence on mental health impacts (Quenby et al., 2021). Indeed, estimates of the magnitude of effect for both anxiety and depression were similar across low, middle and high resource settings.

When outcomes were measured categorically (i.e. on the basis of 'caseness') the association between perinatal loss and depression was slightly stronger than the association between loss and anxiety, although both were significant. Conversely, continuous measurement (mean scores for psychopathology) derived similar effect size estimates for the associations between both loss and anxiety, and loss and depression. This is consistent with a conceptualization of depression and anxiety as 'common mental health disorders', occurring with some degree of overlap, although there are also methodological issues relating to comparing outcomes in the depression and anxiety samples. Both anxiety and depression rates were also elevated in late versus early loss, across both categorical and continuous outcomes. Meta-regression analyses suggested study quality and maternal age did not have a significant effect on depression outcomes. However, higher study quality rating and younger maternal age birth had a small but significant effect on elevated anxiety outcomes.

4.2. Strengths and limitations

We note a number of limitations in our analyses. Although we tried to survey the global status of research in this field, we were limited our search to only English language papers. Additionally, most studies that

Table 3
Quality checklist.

Author(s) (year)	Unbiased selection of perinatal loss cohort?	Selected control minimizes baseline differences in prognostic factors?	Sample size calculated?	Adequate description of the cohort?	Reliable identification of perinatal loss group?	Validated method for ascertaining anxiety, depression and/or PTS?	Outcome assessment blind to exposure?	Adequate follow-up period? (longitudinal studies only)*	Missing data/drop-out at acceptable level?	Analysis controls for confounding predictors/correlates of mental health outcomes?	Analytic methods appropriate?	Total AHRQ Score
Adeyemi et al. (2008)	Partially	Yes- M	No	Yes	Yes	Yes	Can't Tell	N/A	Yes	Yes	Partially	14/20–70
Adib-Rad et al. (2019)	Yes	Partially	No	Yes	Yes	Yes	Can't Tell	N/A	Yes	Yes	Yes	15/20–75
Boyle et al. (1996)	Yes	Yes-M	No	Yes	Yes	Yes	Can't Tell	Yes	Yes	Yes	Yes	18/22–82
Budak et al. (2016)	Partially	Partially	No	Yes	Partially	Yes	Can't Tell	N/A	Can't Tell	Yes	Partially	10/20–50
Chung et al. (2017)	Partially	Partially	Yes	Yes	Partially	Yes	Can't Tell	N/A	Can't Tell	Yes	Yes	13/20–65
Dingle et al. (2008)	Yes	Partially	No	No	Partially	Yes	Can't Tell	N/A	Yes	Yes	Yes	12/20–60
Farren et al. (2016)	Yes	Partially	Yes	Partially	Yes	Yes	Can't Tell	Partially	Yes	Yes	Yes	17/22–77
Filippi et al. (2007)	Yes	Partially	Yes	Yes	Yes	Partially	Can't Tell	Yes	Yes	Yes	Yes	18/22–82
Filippi et al. (2010)	Yes	Partially	No	Yes	Yes	Partially	No	Yes	Yes	Yes	Yes	16/22–73
Gausia et al. (2011)	Yes	Partially	No	Yes	Yes	Yes	Can't Tell	Yes	Can't tell	Yes	Yes	15/22–68
Gold et al. (2014)	Yes	Partially	No	Yes	Yes	Yes	Can't Tell	N/A	Partially	Yes	Yes	14/20–70
Gravensteen et al. (2012)	Yes	Partially	Yes	Yes	Yes	Yes	Can't Tell	N/A	Partially	Yes	Yes	16/20–80
He et al. (2019)	Yes	Partially	No	Yes	Partially	Yes	Can't Tell	N/A	Yes	Yes	Yes	14/20–70
Hogue et al. (2015)	Yes	Partially	No	Yes	Yes	Yes	No	N/A	Partially	Yes	Yes	14/20–70
Isguder et al. (2018)	Yes	Partially	Yes	Yes	Yes	Yes	Can't Tell	N/A	No	Yes	Yes	15/20–75
Jacob et al. (2017)	Yes	Yes-M	Partially	Partially	Yes	Partially	Can't Tell	N/A	Can't Tell	Partially	Yes	12/20–60
Kersting et al. (2009)	Partially	Partially	No	Yes	Yes	Yes	Can't Tell	Yes	Yes	No	Yes	14/22–64
Klier et al. (2000)	Yes	Yes-M	No	Yes	Yes	Yes	Can't Tell	N/A	Yes	Yes	Yes	16/20–80
Kolte et al. (2015)	Yes	Partially	No	Yes	Yes	Yes	Can't Tell	N/A	Yes	Yes	Yes	15/20–75
Kulathilaka et al. (2016)	Yes	Partially	Yes	Yes	Yes	Yes	Can't Tell	N/A	Yes	Partially	Yes	16/20–80
Lewkowitz et al. (2019)	Yes	Partially	Partially	Yes	Yes	Partially	Can't Tell	N/A	Yes	Yes	Yes	15/20–75
Lok et al. (2010)	Partially	Partially	No	Yes	Yes	Yes	Can't Tell	Partially	Yes	Yes	Yes	15/22–68
Ng et al. (2017)	Yes	Yes-M	No	Yes	Yes	Yes	Can't Tell	N/A	Yes	Yes	Partially	15/20–75
Prost et al. (2012)	Yes	Yes	Partially	Yes	Yes	Partially	Partially	N/A	Yes	Yes	Yes	17/20–85
	Yes	Partially	No	Yes	Yes	Yes	Can't Tell	Yes	Yes	Yes	Yes	

(*continued on next page*)

Table 3 (*continued*)

Author(s) (year)	Unbiased selection of perinatal loss cohort?	Selected control minimizes baseline differences in prognostic factors?	Sample size calculated?	Adequate description of the cohort?	Reliable identification of perinatal loss group?	Validated method for ascertaining anxiety, depression and/or PTS?	Outcome assessment blind to exposure?	Adequate follow-up period? (longitudinal studies only)*	Missing data/ drop-out at acceptable level?	Analysis controls for confounding predictors/ correlates of mental health outcomes?	Analytic methods appropriate?	Total AHRQ Score
Rees et al. (2007)												17/ 22–77
Schwerdtfeger et al. (2009)	Yes	Partially	No	Partially	Partially	Yes	Can't Tell	N/A	Can't Tell	Partially	Partially	9/ 20–45
Surkan et al. (2016)	Yes	Yes	Partially	Yes	Yes	Yes	Partially	N/A	Yes	Yes	Yes	18/ 20–90
Tavoli et al. (2018)	Yes	Partially	Yes	Partially	Yes	Yes	Can't Tell	N/A	Can't Tell	Partially	Partially	12/ 20–60
Toffol et al. (2013)	Yes	Partially	Partially	Yes	Partially	Yes	Can't Tell	N/A	Yes	Yes	Yes	15/ 20–75

Note: Numeric values assigned to each grading scale: "Yes" = 2, "Partially" = 1, "No"/"Can't tell" = 0.

satisfied our inclusion criteria were conducted in North America or Western Europe, whereas studies from South America, Southeastern Europe, Africa, and Asia were scarce. Indeed, an extensive 'grey literature' search found no additional un-published papers. Publication bias analysis suggested potentially non-significant studies were missing from the current literature, highlighting limitations in taking a global perspective on these data.

Furthermore, there was substantial heterogeneity in the meta analyses of both continuous and categorical outcomes for depression and anxiety. Moderator analyses also suggested substantial heterogeneity, also compounded by relatively small numbers studies in each sub-group. This is a similar observation to review findings for the impact of perinatal loss on mental health in subsequent pregnancies (Hunter et al., 2017) but does suggest that methodological, demographic and sampling differences hamper the ability to make precision estimates of the mental health sequelae of perinatal loss. One option would be to move towards greater methodological consistency such as standardised assessments of depression, anxiety and stress using a limited number of measures only. Equally, the high heterogeneity may reflect the interaction of different variables (e.g. type of control, type of loss) within different studies. Multivariate meta-analysis could potentially parse out some of this heterogeneity, but given the relatively small number of studies in subgroups, it may simply require the accrual of further study data.

Our analysis was also limited to studies with comparison groups. Although this reduced baseline differences by equating a sample and control group with similar health care access, this criterium excluded many non-controlled studies, particularly in the PTS outcome domain. The analysis also combined effect sizes of studies across diverse designs. Differences in the categorisation of demographic data made comparisons difficult. Only maternal age analyses were possible, which limited the scope of this review. Additionally, moderator analyses were limited by underpowered data within the included studies, and some sub-groups comprised of data provided by a single study. As too few studies adequately reported or controlled for previous births and losses or previous mental health challenges of participants, we were also unable to run a full analysis of these covariates which may have further influenced the summary results.

We also note differences in terminology in the literature around perinatal loss. Within this review, the term "perinatal loss" covered the time-period from conception through to 28 days post-delivery. As the terminology and associated gestational age groups varied between the individual studies, the data was organised into broad categories. This categorisation allowed for an analysis of general trends but also reduced the specificity of outcomes. Our review also did not fully explore the mental health outcomes following TOPFA as only one study was found that satisfied the inclusion criteria. As studies from more conservative countries would have categorised TOPFA under the umbrella of abortion instead of perinatal loss (Center for Reproductive Rights, 2020), suitable papers may have been inadvertently excluded from our analysis at the search stage.

The timing of mental health assessments following perinatal loss also varied significantly between the included papers. While some studies measured mental health outcomes the day following loss (Ng et al., 2017; Isguder et al., 2018), another performed assessments at any time within 7 years following loss (Schwerdtfeger and Shreffler, 2009). This indeterminate time variable not only resulted in a generalised analysis of mental health outcomes, but also limited the scope for analysis of the longitudinal impact of loss on mental health.

4.3. Implications for research and practice

Our analyses suggest a number of directions for future research and practice in this area.

Studies included a variety of loss stages, allowing for analysis of gestational stage to be conducted. Results were found to be consistent with previous research, identifying gestational age as a risk factor for

common mental health disorders (Engelhard et al., 2001; Janssen et al., 1997). Analysis found that following loss, the risk for both depression and anxiety increased with the progression of pregnancy. These overall findings can be linked with current literature exploring the development of attachment between the mother and foetus throughout pregnancy, where symptoms of mental health disorders are more likely to be experienced following late perinatal loss (Grace, 1989; Salahi and Kohan, 2017).

Several studies included within this analysis found an association between recurrent perinatal loss and increased levels of depression compared to women who had not experienced RPL. These women not only experience the physical impact of repeated loss but also the psychological sequelae of infertility and childlessness which can have an enduring effect (deMontigney et al., 2017). Due to the limited number of studies, further exploration into the impact of recurrent loss is a priority.

Study locations ranged from low to high-income countries, with comparisons finding no major differences between the levels of depression or anxiety. Our results suggest a notable level of consistency in estimates of depression and anxiety across Low and Middle resource settings, contradicting outcomes from previous studies (Isguder et al., 2017; Adeyemi et al., 2008; Tavoli et al., 2018). This is surprising given the nesting of mental health within social determinants of mental health and the impact in low resource settings of poverty, financial instability and poor access to care hospitals as risk factors for anxiety amongst women in their reproductive years (Gausia et al., 2011; Filippi et al., 2007). Further, although we found no significant impact for maternal age on depression outcomes, an increase in anxiety levels was associated with a younger maternal age, partially supporting existing research exploring the development of common mental health disorders following perinatal loss (Sham et al., 2010).

Analyses of the different control groups from our studies suggest a greater association between depression and anxiety for women following perinatal loss when they are compared against pregnant women, than when compared with women who had recently given birth and those from the community who are not pregnant. The “live birth” control, however, may not have adequately reduced baseline differences as this group showed a high level of heterogeneity and cannot explain much variance. The results may be additionally confounded by the likelihood that early loss samples are paired with community or pregnant controls and late loss samples are paired with ’live birth’ controls. The finding that the pregnant control group had the smallest effect size could arise from the presence of antenatal depression and anxiety, as explored in Hunter’s meta-analysis (2017). Including women from the community as a control group may also contribute to inaccuracies (Mills et al., 2014), as the level of depression and anxiety amongst this group is not related to gestational outcome (either adverse or positive). Thus, comparing a perinatal loss group with non-pregnant women would naturally yield a larger effect size than with pregnant or “live-birth” controls.

Meta-regression analyses revealed that the quality of the study did not predict the level of anxiety, yet it was shown to predict a medium and significant increase in women’s levels of depression following perinatal loss. Moderator analysis suggested consistency across different diagnostic tools on the prevalence of anxiety and depression. Validated, frequently used questionnaires, such as the EPDS (Bhusal et al., 2016; which has high sensitivity and is specifically designed to detect depression in the postnatal period (Ji et al., 2011)) or the HADS screen for depression and anxiety (Bjelland et al., 2002), seemed to perform similarly other less frequently used, but still validated screens.

As with the general direction of travel around research in perinatal loss (Quenby et al., 2021) our review highlights the importance of harmonising methodologies across studies and cohorts, thus reducing heterogeneity and increasing consistency. Further longitudinal studies are also required to address the evolution of the mental health sequelae of loss over time. A comprehensive understanding of the research limitations by the medical community would also help to reduce incidents of ineffective care at the wrong time or the over-medicalisation of mental health outcomes following loss (Miller et al., 2016). This is also important in the context of the pressure on both health services in general and both maternity and mental health services during the Covid pandemic.

Appropriate and timely mental health education following perinatal loss could greatly benefit women and their partners and aid in their adaptation to this distressing event. Implementation of mental health assistance into the general health services for women following loss would allow for a continuity of care and further assist women who are planning a future pregnancy or those who may be experiencing recurrent loss. Furthermore, a more nuanced understanding of the associated social and cultural risk and protective factors for common mental health disorders following loss could also support planning and implementation of health policies that enable equitable access to maternal mental health care.

Author statement

The study was conceived by AM. Searches, data extraction and initial analyses were completed by KY, DH and MP. The initial draft was created by KY, DH and MP. The final version was edited and approved by all authors.

The study was conducted as part of an MSc dissertation project involving DH, MP and KY, supervised by AM.

Ethics approval

The University of Edinburgh did not require ethics approval for this review as recruitment of new participants was not necessary to perform this meta-analysis.

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Declaration of Competing Interest

AM is a member of the steering group for the NHS Scotland Managed Care Network for Perinatal Mental Health and an adviser to the NHS Education Scotland Perinatal Mental Health Psychological Therapies Matrix . DH, MP and KY have no conflicts of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2021.10.026.

References

Adeyemi, A., Mosaku, K., Ajenifuja, O., Fatoye, F., Makinde, N., Ola, B., 2008. Depressive symptoms in a sample of women following perinatal loss. J. Natl. Med. Assoc. 100 (12), 1463–1468.

Adib-Rad, H., Basirat, Z., Faramarzi, M., Mostafazadeh, A., Bijani, A., 2019. Psychological distress in women with recurrent spontaneous abortion: a case-control study. Turk. J. Obstet. Gynecol. 16, 151–157.

Adolfsson, A., 2011. Meta-analysis to obtain a scale of psychological reaction after perinatal loss: focus on miscarriage. Psychol. Res. Behav. Manag. 4, 29–39.
Armstrong, D.S., 2004. Impact of prior perinatal loss on subsequent pregnancies. J. Obstet. Gynecol. Neonatal. Nurs. 33, 765–773.
Bhusal, B.R., Bhandari, N., Chapagai, M., Gavidia, T., 2016. Validating the Edinburgh Postnatal Depression Scale as a screening tool for postpartum depression in Kathmandu, Nepal. Int. J. Ment. Health Syst. 10 (1), 1–7.
Bjelland, I., Dahl, A.A., Haug, T.T., Neckelmann, D., 2002. The validity of the Hospital Anxiety and Depression Scale: an updated literature review. J. Psychosom. Res. 52 (2), 69–77.
Borenstein, M., 2009. Introduction to meta-analysis. Statistics in Practice. John Wiley & Sons, Chichester, U.K.
Boyle, F.M., Vance, J.C., Najman, J.M., Thearle, M.J., 1996. The mental health impact of stillbirth, neonatal death or sids: prevalence and patterns of distress among mothers. Soc. Sci. Med. 43 (8), 1273–1282.
Brier, N., 2004. Anxiety after miscarriage: a review of the empirical literature and implications for clinical practice. Birth 31, 138–142.
Budak, A.M.U., Harris, G., Blissett, J., 2016. Perinatal trauma with and without loss experiences. J. Reprod. Infant. Psychol. 34 (4), 413–425.
Burden, C., Bradley, S., Storey, C., Ellis, A., Heazell, A.E.P., Downe, S., Cacciatore, J., Siassakos, D., 2016. From grief, guilt pain and stigma to hope and pride - a systematic review and meta-analysis of mixed-method research of the psychosocial impact of stillbirth. BMC Pregnancy Childbirth 16, 9.
Center for Reproductive Rights. (2020). *The world's abortion laws*. Retrieved from https://maps.reproductiverights.org/worldabortionlaws. [Accessed 08/06/2020].
Christiansen, D.M., 2017. Posttraumatic stress disorder in parents following infant death: a systematic review. Clin. Psychol. Rev. 51, 60–74.
Chung, M.C., Reed, J., 2017. Posttraumatic stress disorder following stillbirth: trauma characteristics, locus of control, posttraumatic cognitions. Psychiatr. Q. 88 (2), 307–321.
Daugirdaitė, V., van den Akker, O., Purewal, S., 2015. Posttraumatic stress and posttraumatic stress disorder after termination of pregnancy and reproductive loss: a systematic review. J. Pregnancy 2015.
deMontigny, F., Verdon, C., Meunier, S., Dubeau, D., 2017. Women's persistent depressive and perinatal grief symptoms following a miscarriage: the role of childlessness and satisfaction with healthcare services. Arch. Womens Ment. Health 20 (5), 655–662.
DerSimonian, R., Laird, N., 1986. Meta-analysis in clinical trials. Control Clin. Trials 7, 177–188.
Dingle, K., Alati, R., Clavarino, A., Najman, J.M., Williams, G.M., 2008. Pregnancy loss and psychiatric disorders in young women: an Australian birth cohort study. Br. J. Psychiatry 193 (6), 455–460.
Duval, S., Tweedie, R., 2000. A nonparametric "trim and fill" method of accounting for publication bias in meta-analysis. J. Am. Stat. Assoc. 95, 89–98.
Engelhard, I.M., van den Hout, M.A., Arntz, A., 2001. Posttraumatic stress disorder after pregnancy loss. Gen. Hosp. Psychiatry 23 (2), 62–66.
Farquharson, R.G., Jauniaux, E., Exalto, N., 2005. Updated and revised nomenclature for description of early pregnancy events. Hum. Reprod. 20 (11), 3008–3011.
Farren, J., Jalmbrant, M., Ameye, L., Joash, K., Mitchell-Jones, N., Tapp, S., Timmerman, D., Bourne, T., 2016. Post-traumatic stress anxiety and depression following miscarriage or ectopic pregnancy: a prospective cohort study. BMJ Open 6, e011864.
Farren, J., Mitchell-Jones, N., Verbakel, J.Y., Timmerman, D., Jalmbrant, M., Bourne, T., 2018. The psychological impact of early pregnancy loss. Hum. Reprod. Update 24 (6), 731–749.
Filippi, V., Ganaba, R., Baggaley, R.F., Marshall, T., Storeng, K.T., Sombié, I., Ouattara, F., Ouedraogo, T., Akoum, M., Meda, N., 2007. Health of women after severe obstetric complications in Burkina Faso: a longitudinal study. Lancet North Am. Ed. 370 (9595), 1329–1337.
Filippi, V., Goufodji, S., Sismanidis, C., Kanhonou, L., Fottrell, E., Ronsmans, C., Alihonou, E., Patel, V., 2010. Effects of severe obstetric complications on women's health and infant mortality in Benin: effects of severe obstetric complications. Trop. Med. Int. Health 15 (6), 733–742.
Gausia, K., Moran, A.C., Ali, M., Ryder, D., Fisher, C., Koblinsky, M., 2011. Psychological and social consequences among mothers suffering from perinatal loss: perspective from a low income country. BMC Public Health 11 (1), 1–9.
Gold, K.J., Boggs, M.E., Muzik, M., Sen, A., 2014. Anxiety disorders and obsessive compulsive disorder 9 months after perinatal loss. Gen. Hosp. Psychiatry 36 (6), 650–654.
Grace, J.T., 1989. Development of maternal-fetal attachment during pregnancy. Nurs. Res.
Gravensteen, I.K., Helgadottir, L.B., Jacobsen, E.-.M., Sandset, P.M., Ekeberg, Ø., 2012. Long-term impact of intrauterine fetal death on quality of life and depression: a case–control study. BMC Pregnancy Childbirth 12 (1), 43.
He, L., Wang, T., Xu, H., Chen, C., Liu, Z., Kang, X., Zhao, A., 2019. Prevalence of depression and anxiety in women with recurrent pregnancy loss and the associated risk factors. Arch. Gynecol. Obstet. 300 (4), 1061–1066.
Higgins, J.P., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M.J., Welch, V.A., 2019. Cochrane Handbook For Systematic Reviews of Interventions. John Wiley & Sons.
Hogue, C.J.R., Parker, C.B., Willinger, M., Temple, J.R., Bann, C.M., Silver, R.M., … Goldenberg, R.L., 2015. The association of stillbirth with depressive symptoms 6-36 months post-delivery. Paediatr. Perinat. Epidemiol. 29 (2), 131–143.
Hunter, A., Tussis, L., MacBeth, A., 2017. The presence of anxiety, depression and stress in women and their partners during pregnancies following perinatal loss: a meta-analysis. J. Affect. Disord. 223, 153–164.
Isguder, C.K., Batmaz, S., Yildiz, M., Songur, E., Dogru, H.Y., Delibas, I.B., Cakmak, B., Ozsoy, A.Z., 2018. Relationship between miscarriage and dysfunctional cognitions about trauma, coping mechanisms, and posttraumatic growth. J. Ratio.-Emotive Cogn.-Behav. Therapy 36, 99–118.
Jacob, L., Polly, I., Kalder, M., Kostev, K., 2017. Prevalence of depression, anxiety, and adjustment disorders in women with spontaneous abortion in Germany - A retrospective cohort study. Psychiatry Res. 258, 382–386.
Janssen, H.J., Cuisinier, M.C., de Graauw, K.P., Hoogduin, K.A., 1997. A prospective study of risk factors predicting grief intensity following pregnancy loss. Arch. Gen. Psychiatry 54 (1), 56–61.
Ji, S., Long, Q., Newport, D.J., Na, H., Knight, B., Zach, E.B., …, Stowe, Z.N., 2011. Validity of depression rating scales during pregnancy and the postpartum period: impact of trimester and parity. J. Psychiatr. Res. 45 (2), 213–219.
Kersting, A., Kroker, K., Steinhard, J., Hoernig-Franz, I., Wesselmann, U., Luedorff, K., … Suslow, T., 2009. Psychological impact on women after second and third trimester termination of pregnancy due to fetal anomalies versus women after preterm birth-a 14-month follow up study. Arch. Women Ment. Health 12 (4), 193–201.
Klier, C.M., Geller, P.A., Neugebauer, R., 2000. Minor depressive disorder in the context of miscarriage. J. Affect. Disord. 59, 13–21.
Kulathilaka, S., Hanwella, R., de Silva, V.A., 2016. Depressive disorder and grief following spontaneous abortion. BMC Psychiatry 16 (1), 1–6.
Lancet. (2016). Ending preventable stillbirths. Retrieved from https://www.thelancet.com/pb/assets/raw/Lancet/stories/series/stillbirths2016-exec-summ.pdf [Accessed 30/07/2020].
Lawn, J.E., Blencowe, H., Waiswa, P., Amouzou, A., Mathers, C., Hogan, D., …, Draper, E.S., 2016. Stillbirths: rates, risk factors, and acceleration towards 2030. Lancet (British edition) 387 (10018), 587–603.
Lewkowitz, A.K., Rosenbloom, J.I., Keller, M., López, J.D., Macones, G.A., Olsen, M.A., Cahill, A.G., 2019. Association between stillbirth ≥23 weeks gestation and acute psychiatric illness within 1 year of delivery. Am. J. Obstet. Gynecol. 221 (5), 491 e1-491.e22.
Lok, I.H., Yip, A.S.K., Lee, D.T.S., Sahota, D., Chung, T.K.H., 2010. A 1-year longitudinal study of psychological morbidity after miscarriage. Fertil. Steril. 93 (6), 1966–1975.
Miller, S., Abalos, E., Chamillard, M., Ciapponi, A., Colaci, D., Comandé, D., …, Althabe, F., 2016. Beyond too little, too late and too much, too soon: a pathway towards evidence-based, respectful maternity care worldwide. Lancet North Am. Ed. 388 (10056), 2176–2192.
Mills, T.A., Ricklesford, C., Cooke, A., Heazell, A.E.P., Whitworth, M., Lavender, T., 2014. Parents' experiences and expectations of care in pregnancy after stillbirth or neonatal death: a metasynthesis. BJOG 121 (8), 943–950.
Ng, B.K., Chuah, J.N., Lim, P.S., Shuhaila, A., Marhani, M., Azlin, M.I.N., 2017. Case control study of anxiety and depression among patients with miscarriage compared to those with successful pregnancy. Med. Health-Kuala Lumpur 12, 244–258.
Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D., Shamseer, L., Tetzlaff, J.M., Akl, E.A., Brennan, S.E., Chou, R., Glanville, J., Grimshaw, J.M., Hróbjartsson, A., Lalu, M.M., Li, T., Loder, E.W., Mayo-Wilson, E., McDonald, S., McGuinness, L.A., Stewart, L.A., Thomas, J., Tricco, A.C., Welch, V.A., Whiting, P., Moher, D., 2021. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ n71.
Price, S.K., McLeod, D.A., 2012. Definitional distinctions in response to perinatal loss and fertility barriers. Illness Crisis Loss 20, 255–273.
Prost, A., Lakshminarayana, R., Nair, N., Tripathy, P., Copas, A., Mahapatra, R., Rath, S., Gope, R.K., …, Costello, A., 2012. Predictors of maternal psychological distress in rural India: a cross-sectional community-based study. J. Affect. Disord. 138 (3), 277–286.
Quenby, S., Gallos, I.D., Dhillon-Smith, R.K., Podesek, M., Stephenson, M.D., Fisher, J., …, Coomarasamy, A., 2021. Miscarriage matters: the epidemiological, physical, psychological, and economic costs of early pregnancy loss. Lancet North Am. Ed. 397 (10285), 1658–1667.
Rees, D.I., Sabia, J.J., 2007. The relationship between abortion and depression: new evidence from the fragile families and child wellbeing study. Med. Sci. Monit. 13, CR430–CR436.
Salehi, K., Kohan, S., 2017. Maternal-fetal attachment: what we know and what we need to know. Int. J. Pregnancy Child Birth 2 (5), 146–148.
Schwarzer, G., 2016. Meta: general package for meta-analysis. R Package version 4, 4-0.
Schwerdtfeger, K.L., Shreffler, K.M., 2009. Trauma of pregnancy loss and infertility among mothers and involuntarily childless women in the United States. J. Loss Trauma 14 (3), 211–227.
Sham, A.K.H., Yiu, M.G.C., Ho, W.Y.B., 2010. Psychiatric morbidity following miscarriage in Hong Kong. Gen. Hosp. Psychiatry 32 (3), 284–293.
Stroup, D.F., Berlin, J.A., Morton, S.C., Olkin, I., Williamson, G.D., Rennie, D., Moher, D., Becker, B.J., Sipe, T.A., Thacker, S.B., 2000. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 283, 2008–2012.
Surkan, P.J., Sakyi, K., Strobino, D.M., Mehra, S., Labrique, A., Ali, H., …, Christian, P., 2016. Depressive symptoms in mothers after perinatal and early infant loss in rural Bangladesh: a population-based study. Ann. Epidemiol. 26 (7), 467–473.
Tavoli, Z., Mohammadi, M., Tavoli, A., Moini, A., Effatpanah, M., Khedmat, L., Montazeri, A., 2018. Quality of life and psychological distress in women with recurrent miscarriage: a comparative study. Health Qual. Life Outcomes 16 (1), 1–5.
Toffol, E., Koponen, P., Partonen, T., 2013. Miscarriage and mental health: results of two population-based studies. Psychiatry Res. 205 (1–2), 151–158.
Viechtbauer, W., 2010. Conducting meta-analyses in R with the metafor Package. J. Stat. Softw. 36, 1–48.
Williams, J.W., Plassman, B.L., Burke, J., Holsinger, T., Benjamin, S., 2010. Preventing Alzheimer's Disease and Cognitive Decline. Evid. Rep. Technol. Assess. (Full Rep)

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