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REVIEW

Maternal psychosocial consequences of twins and multiple births following assisted and natural conception: a meta-analysis



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Abstract The aim of this meta-analysis is to provide new evidence on the effects on maternal health of multiple births due to assisted reproductive technology (ART). A bibliographic search was undertaken using PubMed, PsycINFO, CINAHL and Science Direct. Data extraction was completed using Cochrane Review recommendations, and the review was performed following PRISMA and MOOSE guidelines. Meta-analytic data were analysed using random effects models. Eight papers (2993 mothers) were included. Mothers of ART multiple births were significantly more likely to experience depression (standardized mean difference [SMD] $d = 0.198$, 95% CI 0.050 – 0.345, $z = 2.623$, $P = 0.009$; heterogeneity $I^2 = 36.47\%$), and stress (SMD $d = 0.177$, 95% CI 0.049 – 0.305, $P = 0.007$; heterogeneity $I^2 = 0.01\%$) than mothers of ART singletons. No difference in psychosocial distress (combined stress and depression) (SMD $d = 0.371$, 95% CI –0.153 – 0.895; $I^2 = 86.962\%$, $P = 0.001$) or depression ($d = 0.152$, 95% CI –0.179 – 0.483; $z = 0.901$; $I^2 = 36.918\%$) were found between mothers of ART and naturally conceived multiple births. In conclusion, mothers of ART multiple births were significantly more likely to have depression and stress than mothers of ART singletons, but were no different from mothers of naturally conceived multiples. [RBM Online](https://doi.org/10.1016/j.rbmo.2016.04.009)

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Introduction

Multiple pregnancy has been recognized as the greatest health risk to both infant and mother following natural conceptions and assisted reproductive technology, such as IVF (HFEA, 2009a). In order to lower the risks of multiple births through assisted conception, guidelines, elective single embryo transfer policies (eSET) and consensus statements have been introduced internationally (e.g. ASRM, 2012; CDC, 2014; ESHRE consensus statement 2002 (Land and Evers, 2003); HFEA, 2009a, 2009b; Min et al., 2010; One at a Time, 2010). Mandatory adoption of eSET in some countries resulted in significant reductions of multiple births (e.g. Bissonnette et al., 2011) and perinatal mortality (Sullivan et al., 2012).

Much research on multiple births has emphasized maternal and infant mortality and medical morbidity, particularly in assisted reproductive technology multiples (Ezugwu and Van der Burg, 2015). Less research has focused on maternal stress during pregnancy and psychosocial morbidity following (particularly prematurely delivered) multiple pregnancies. According to the fetal programming hypothesis (Egliston et al., 2007), maternal stress during pregnancy can alter the development of the fetus, especially of the brain. Post-partum, multiple births can lead to maternal isolation, depression and, in extreme cases, child abuse (Ombelet et al., 2005). Furthermore, evidence also suggests that assisted reproductive technology multiple births are associated with greater psychological problems compared with assisted reproductive technology singleton births (e.g., Ellison et al., 2005; Olivennes et al., 2005; Vilska et al., 2009), but there are exceptions (Sydsjö et al., 2008). The evidence linking increased risks for depression in mothers of twins is generally well supported for assisted reproductive technology multiples (Vilska and Unkila-Kallio, 2010) and natural conception multiples (Ross et al., 2011). Ross et al.'s (2011) systematic review reported that mothers of twins/multiples were likely to be at a higher risk for symptoms of post-partum depression. However, the authors did not clearly differentiate between the two possible control/comparison groups (mothers who conceived twins or multiples naturally and mothers who conceived singletons via assisted reproductive technology). Most of the available literature examined maternal psychological functioning after assisted reproductive technology multiples, and there were insufficient data to perform meta-analysis on paternal psychological functioning after assisted reproductive technology multiples (Vilska et al., 2009).

In studies comparing assisted reproductive technology twins/multiples with natural conception twins/multiples, no differences in maternal psychological functioning have generally been found (e.g. Colpin et al., 1999; Tully et al., 2003; Vilska et al., 2009). Others have reported more psychological distress in mothers of assisted reproductive technology twins/multiples than in mothers of natural conception twins/multiples (Baor et al., 2004; Yokoyama, 2003). These differences may be due to a higher risk of depression and marital decline in assisted reproductive technology mothers (Klock, 2004). Research revolving around marital satisfaction among assisted reproductive technology mothers of multiples and singletons is conflicting. While some studies report no difference between these two groups (Olivennes et al., 2005), others support the hypothesis that a multiple birth decreases marital satisfaction among assisted reproductive tech-

nology mothers (Roca de Bes et al., 2009, 2011). Ellison et al. (2005) reported a similar tendency, although the findings were not statistically significant. However, it seems that some assisted reproductive technology multiple mothers tend to cope well with the strain and do not divorce more often than mothers of singletons (Pinborg et al., 2003). Many previous reviews are now over 10 years old (Bryan, 2002; Klock, 2004), are narrative reviews (McGrath et al., 2010; Vilska and Unkila-Kallio, 2010), considered twins/multiples briefly (Hammarberg et al., 2008), focused solely on depression as the outcome variable (Ross et al., 2011) and did not control for multiplicity (Gressier et al., 2015). There is a need for other psychological consequences of post-natal emotional adjustment to be examined to gain a better understanding of the complex and multifactorial nature of the post-natal psychological state of women who conceive using assisted reproductive technology and have multiple births.

Therefore, the aim of this study is to reconcile the previous research literature on the psychological consequences of twins/multiple births after assisted reproductive technology. Given the clinical implications of assisted reproductive technology multiple births, this meta-analytic and review process extrapolates the research evidence by comparing depression, anxiety and stress of assisted reproductive technology twins/multiples mothers versus natural conception twins/multiples mothers and assisted reproductive technology twins/multiples mothers versus assisted reproductive technology singleton mothers. Following the theoretical background, the meta-analysis was based on the following hypotheses: (i) mothers of assisted reproductive technology twins/multiples will report more psychological problems (depression, anxiety and stress) than mothers of assisted reproductive technology singletons; (ii) natural conception twins/multiples mothers will report fewer psychological problems than assisted reproductive technology mothers of twins/multiples.

Materials and methods

Searches were carried out by all three investigators, who all had previous experience of systematic reviewing and meta-analytic techniques.

Search strategy

This systematic review and meta-analysis was organized and structured according to the PRISMA and MOOSE guidelines (Stroup et al., 2000). A bibliographic search for publications was undertaken using PubMed, PsycINFO, CINAHL and Science Direct. Dates of publication ranged from 1976 to September 2014. The search was augmented with hand searches of articles cited in reference lists and from relevant review papers (e.g. Ross et al., 2011). Most of the databases included the following keywords: ("postpartum" OR "postnatal" OR "pregnan*" OR "perinatal" OR "childbirth" OR "obstetr*" OR "labour" OR "puerperal" OR "parturition" OR "parity" OR "maternal") and ("multiple births" OR "twins" OR "triplets") and ("psychological stress" OR "depressive disorder" OR "anxiety" OR "anxiety disorder" OR "adjustment disorder" OR

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