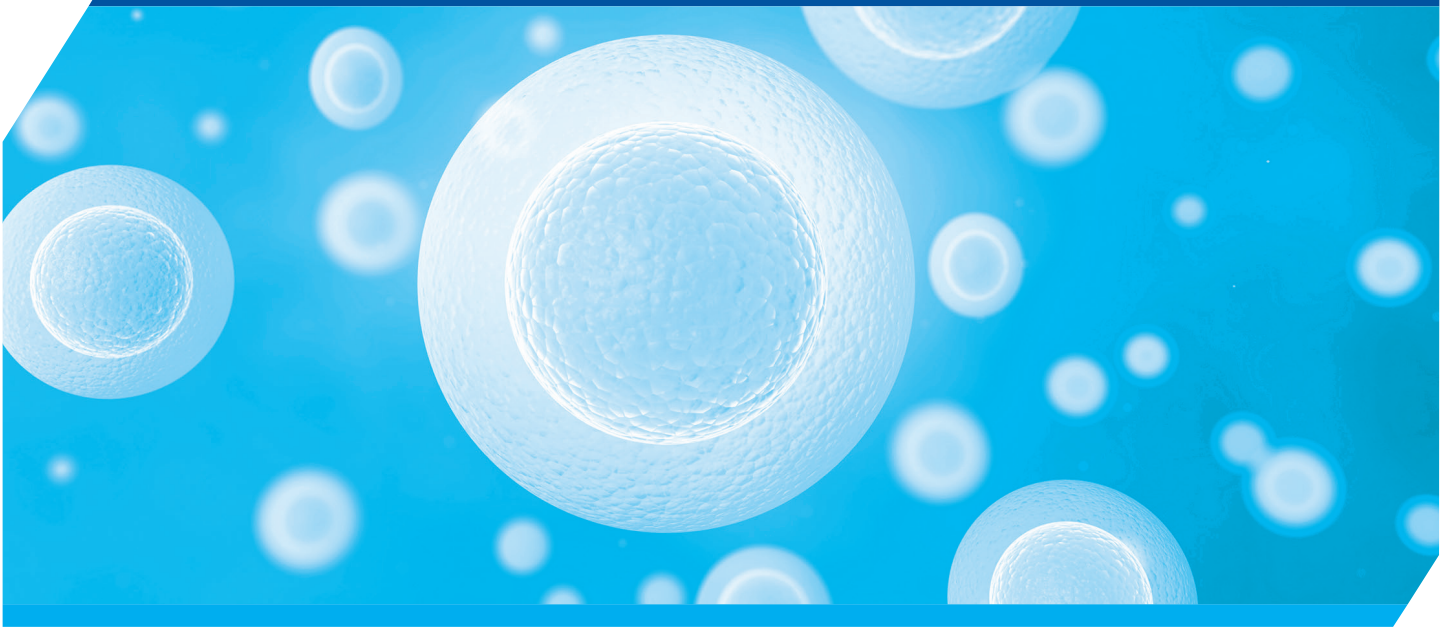
The Fertility Society of Australia

Pre-Conception Health Special Interest Group



Effects of mental illness and its treatment on fertility and pregnancy health

Optimum pre-conception health, including mental health, increases the chance of conceiving spontaneously and with assisted reproductive technology (ART) and reduces the risk of obstetric and neonatal complications. It is also linked to a better long-term health trajectory for the offspring. Common mental disorders (CMD), including depression and anxiety, are associated with poorer physical health. This is thought to be due to a range of factors including a likely increase in inflammatory responses and higher rates of lifestyle behaviours such as smoking, risky levels of alcohol use, obesity, poor nutrition and low physical activity among people with CMD who are also less likely than people who are well to seek appropriate healthcare. Healthcare professionals who care for women in their reproductive years need to be aware of the importance of optimising pre-conception health and how to assess and manage the mental and physical health of women with CMD who are pregnant or plan a pregnancy. Evidence about the effects of mental illness and its treatment on fertility and pregnancy health is reviewed.

Your fertility

Your Fertility is a national public education program funded by the Australian Government Department of Health.

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In Australia about one in five women will experience depression and one in three anxiety in their lifetime. For women with mild symptoms of CMD who wish to conceive, pre-conception health may be optimised through advice about and support to adopt healthy lifestyle behaviours, including folate intake, and brief psychological interventions. For those with moderate or severe depression and anxiety, ongoing pharmacological treatments may also be needed. Women who experience depression and anxiety as a relapsing disorder associated with significant impact on functioning and suicidal ideation or attempts should be managed by a psychiatrist. They may require ongoing treatment with medications including anti-depressants and, more rarely, mood stabilisers (e.g. lithium, lamotrigine) or antipsychotic medications. Women with severe depression and anxiety have poorer physical health and are more likely than women who are well to be vitamin D deficient and less likely to take pregnancy multivitamins and folate leading up to and during pregnancy. They need ongoing and comprehensive support to manage their physical and mental health to reduce the risks of their mental illness on fertility and pregnancy health.

In the context of fertility treatment and pregnancy, the mental health of the male partner is also important. Men who suffer mental illness may have reduced capacity to support their partner through fertility treatment, pregnancy and early parenting, and the condition may adversely affect their transition to fatherhood. There is enough evidence that paternal depression negatively affects partner health and parenting capacity to recommend assessment of the male partner's mental health and referral for treatment if needed as part of fertility and pregnancy healthcare [1]. As with women with depression, men with untreated or undertreated depression may also be prone to unhealthy lifestyle behaviours, such as smoking and excessive alcohol use, which are associated with reduced fertility, increased risks of pregnancy complications and health problems in the offspring. Men who have ongoing significant mental disorders requiring pharmacological treatment are advised to discuss with their treating doctor any potential implications of their condition and its treatment on their fertility and offspring's health. Assessment of paternal mental health should be part of holistic fertility management.

Evidence review

Fertility and ART outcomes

Untreated depression and anxiety are associated with higher smoking rates and risky levels of alcohol use, both of which adversely affect fertility [2]. A study examining the impact of antidepressant use on natural fertility found that women on medication were less likely to conceive than women who were not but did not fully account for the effects that depression or anxiety might have had on this finding [3]. A recent systematic review found no difference between those who took antidepressant medication and those who did not on assisted reproductive treatment (ART) outcomes including peak levels of follicle stimulating hormone (FSH) and estradiol, number of oocytes retrieved, number of embryos transferred and implantation rates [4]. A study following this review examined the impact of depression/anxiety (managed with selective serotonin reuptake inhibitors [SSRIs], managed with non-SSRIs, or untreated) on live birth rates following ART. In this study of 23,557 Swedish women undergoing their first IVF cycle, 4.4 per cent had been diagnosed with depression/anxiety and/or dispensed antidepressants. Those taking SSRIs had similar live birth rates to the background population. However, women taking a non-SSRI (e.g. tricyclic antidepressants, mirtazapine, venlafaxine, duloxetine, agomelatine) and those with untreated depression had a significantly lower live birth rate [5]. Similarly, an earlier study of Danish women found untreated depression and anxiety significantly reduced the rate of live births following ART [6].

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Pregnancy outcomes

Depression and anxiety are amongst the most common complications of pregnancy and the postpartum. Prevalence rates range between seven per cent and 13 per cent depending on timing of assessment and measure used; in particular whether a screening measure or diagnostic interview was used [3, 7]. For those with pre-existing depression and anxiety relapse in pregnancy and/or the postpartum is not uncommon. Studies of the role of antidepressant treatment in preventing relapse in those with pre-existing depression have yielded conflicting results. One study [8] found that the risk of relapse did not increase when treatment for depression was ceased in pregnancy while another study found higher rates of relapse in those who discontinued medication than in those who did not (68 per cent versus 26 per cent) [9]. Furthermore, a 31 per cent increased risk of developing suicidal ideation was identified following abrupt discontinuation of antidepressants in early pregnancy [10]. This latter finding is of particular concern given the high rates of cessation of medication in early pregnancy found in community samples [11, 12].

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The question often is not whether to treat but instead how to treat women with clinically significant depression or anxiety optimally before and during pregnancy. What is clear is that they should be treated with the minimal effective dose of any medication used and that the emphasis needs to be upon effective rather than minimal. What needs to be avoided is acceptance of the risks of both non-treatment and of partial treatment. Where possible, monotherapy is preferable to polypharmacy.

Risks of non-treatment

A meta-analysis of perinatal outcomes for women diagnosed with depression and anxiety in pregnancy has shown an increased risk of preterm delivery and decreased rates of breastfeeding initiation [13]. Maternal depression and anxiety in pregnancy may also adversely affect subsequent infant emotional and cognitive development although the mechanisms for this remain unknown [14].

Risks of treatment

When considering the risks of pharmacological treatment in pregnancy four main areas need to be considered:

1. Does the medication increase the malformation rate above the two to four per cent observed in the general population?

2. Does the medication compromise or complicate pregnancy in any way (such as increase the risk of miscarriage, gestational diabetes, prematurity etc.)?

3. Is the neonate likely to experience any adverse effects from medication exposure at birth (such as withdrawal effects, sedation, or other aspects of neonatal adaption)?

4. What are the longer-term risks for a child in terms of adverse neurodevelopmental or other health outcomes?

While evidence on outcomes of antidepressant exposure in utero is emergent, it suggests an association with increased risk of preterm delivery and lower Apgar scores [15]. Overall, exposure does not appear to be associated with an increased risk of major malformations, although the possible association between the use of paroxetine and cardiac malformations is unclear [16]. Evidence about associations between SSRI antidepressant exposure in utero and persistent pulmonary hypertension of the newborn (PPHN) is inconclusive [17]. Poor neonatal adaptation is found in some infants exposed to SSRIs in late pregnancy [18]. Evidence about long term neurodevelopmental outcomes is inconclusive but suggest that antidepressant exposure in utero is not associated with poorer cognitive outcomes [19]. While there have been some reports of a small increased risk of autism resulting from antidepressant exposure, findings across studies are inconsistent. For all identified associations between antidepressant in utero exposure and adverse neonatal outcomes, the effect sizes are small [15, 16].

Informed consent

Inevitably, at some point, difficult decisions need to be made about the management of mental illness in pregnancy and ideally these should involve a collaborative approach between clinician and patient. It is essential that a procedure for obtaining informed consent is followed and patient preference taken into account in the decision-making process. The risks of treatment need to be weighed against the risks of non-treatment to both mother and child. Patients need to know if the proposed treatment can be considered standard practice and what the known risks are. Any specific concerns patients have should also be addressed. Whilst it is not legally required, it is useful for partners to be involved in the decision-making process when appropriate.

Summary & recommendations

The risks of current or proposed treatment needs to be individually assessed for all women being treated for a mental illness who are pregnant or plan pregnancy. To ensure the best possible outcomes both clinicians and patients need to be fully informed and a process of open disclosure regarding what is known and not known regarding risks of treatment and non-treatment followed.

There is growing evidence that both maternal mental illness and its treatment can affect fertility and pregnancy outcomes. A risk-free scenario does not exist and invariably a decision needs to be made regarding initiating or maintaining pharmacological treatment of a mental illness in the context of pregnancy or a planned pregnancy. A risk-benefit analysis needs to occur which considers risks to both the mother and the fetus arising from treatment and non-treatment. An active, rather than passive decision should be made, and a process of obtaining informed consent followed. Ideally these discussions should occur prior to conception.

For more information about pre-conception health visit

The Fertility Society of Australia Your fertility

www.yourfertility.org.au

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