because only these figures show the real efficiency of the program (Veleva et al., 2009).

One of the main findings in the present study was that even among older women there is a wide variation in the prognosis of the treatment (Niinimäki et al., 2012). As well as in any other age group, it is possible to select good prognosis women for eSET and at the same time maintain a good pregnancy rate as well as low multiple pregnancy rate. In our opinion, it is very important to maintain a low risk of multiple pregnancies among women over 40 years of age as women in advanced age have clearly increased risk of preeclampsia, impaired glucose tolerance and obesity than younger women (Lamminpää et al., 2012). We find that it would be irrational, or even unethical, to accept higher multiple birth rate among older women, if it is avoidable.

We want to emphasize that our study was not randomized, and the two groups [eSET and double-embryo transfer (DET)] were highly selected by design. Therefore, the two study groups were not equal regarding the prognostic factors. Hence, the low number of twins in the DET group only indicated that the criteria for eSET or DET were feasible in the clinical practice, and not that DET would be a good option in all women in that age group.

At our clinic all couples were carefully counselled by an experienced doctor on the benefits and risks concerning SET and DET in their particular situation. The opinion of the patients was taken into account and DET was performed if this was the wish of the couple and there were no medical contraindication for a twin pregnancy. We disagree with Gleicher (2012), that our patients’ preferences would have been ignored for the sake of eSET policy.

As stated in our paper, eSET should not be recommended to all IVF patients. The proportion of women suitable for eSET is lower among older age groups, as was also shown in this study. However, if the aim is to decrease risks and thus the number of multiple births, the advantages of eSET have been shown in many countries. By allowing two or even more high-quality embryos to be transferred among older women would expose many women to excessive risk of multiple birth and possible pregnancy complications.

During the last 10 years eSET policy has been adopted in many countries. As far as we know nowhere a drop of overall success rate has been reported while the safety of the treatment, including perinatal outcome, has been significantly improved.

Our study shows that the same criteria as for performing eSET in younger women can also be applied to women older than 40, which could encourage clinics to expand their indications for eSET. We look forward to see if our experience will be confirmed by other investigators. By sharing experiences of different treatment policies it is possible to find the optimal treatment mode in this challenging patient population.

**References**

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**Risks of untreated depression outweigh any risks of SSRIs**

Sir,

A recently published article (Domar et al., 2013) is misleading and harmful. We belong to a worldwide network of professionals who treat psychiatric illness in pregnancy and post-partum and we conclude that, aside from a possible slightly increased risk of miscarriage, selective serotonin re-uptake inhibitors (SSRIs) are relatively safe for use in pregnancy and post-partum (Einarson et al., 2009a,b).

SSRI use in pregnancy is usually considered in the setting of a moderate–severe depressive disorder, not in the context of depressive symptoms associated with infertility. The risk of relapse of depression for those who stop using psychotropic medication during pregnancy is 68% (Cohen et al., 2006). Prenatal depression can lead to missed obstetric appointments, poor diet and sleep, substance abuse and an increased risk of suicide. Women with untreated depression during pregnancy have an increase in preterm births and low birthweight babies due to the depression itself (Wisner et al., 2009). Grote et al. (2010) found delivery dates of 38.5 weeks for those on SSRIs versus 39.4 weeks for depressed women not taking medication and 39.7 weeks for controls, a finding of questionable clinical significance. Therefore, untreated prenatal depression is not beneficial for either the mother or baby.

Concerning the ‘neonatal syndrome’ found in some newborns taking SSRIs, Moses-Kolko et al. (2005) found 10–30% of neonates exposed to SSRIs in utero experienced increased muscle tone, tremulousness, jitteriness, and feeding and sleep problems as well as respiratory difficulties. However, the majority of the infants experienced transient, mild effects that required only supportive care and spontaneously resolved by 2 weeks of age, far better than the infant being cared for by a woman with a severe post-partum depression.

Pulmonary hypertension of the newborn (PPHN) is a serious but rare disorder. The study by Chambers et al. (2006) that first indicated an association between third trimester use of SSRIs study included only 14 cases and 6 controls and relied on after-the-fact patient interviews and incomplete records. 99.5% of the case
infants had no problems. Of the five follow-up studies, two reported an association while three did not (Robinson, 2012). In a critical review of all of these studies, Ochiogrosso et al. (2012) found that it is extremely difficult to differentiate the contribution of SSRIs from that of depression itself. Many of the risk factors for PPHN such as obesity, smoking, reduced length of gestation and Cesarean birth are also found more commonly in depressed women. In conclusion, evidence for an association between SSRI use in the last trimester and PPHN is very weak and must be balanced against the known risks of untreated depression.

Nulman et al. (2011) reviewed studies of the long-term cognitive effects on children whose mothers took antidepressants during pregnancy. Results on more than 1000 children in different studies found antidepressant medication did not affect the children’s global IQ, language development, behavior IQ or temperament during preschool and early school years. Maternal depression, however, resulted in less cognitive and language achievement.

Our group knows well the problem of selectively and uncritically viewing only research that supports a negative view of the use of medication during pregnancy. While cognitive therapy or IPT can be beneficial for women experiencing prenatal depression, those of us who can prescribe medication also understand that, weighing the risk/benefit of untreated depression during pregnancy versus using medication, antidepressant medication can be an important component of treating the pregnant woman and protecting the baby from harm.

References


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Reply: Risks of untreated depression outweigh any risks of SSRIs

Sir,

We appreciate Dr Robinson and Ms Einarson’s interest in our paper and their letter. We have a number of clarifications/explanations about their comments.

The section in our paper on antidepressants and pregnancy is based on fact, not opinion. We make three basic points: (i) there is evidence of risk with the use of SSRI antidepressants by pregnant women; (ii) there is no evidence of improved pregnancy outcomes with the SSRI antidepressants and (iii) pregnant women, providers and the public should be aware of this.

SSRI antidepressants have not been shown to improve pregnancy outcomes and they are increasingly associated with risk. The conventional wisdom has been that depressed pregnant women, by taking SSRI antidepressants, will treat their condition and improve their pregnancy outcomes. But there is no evidence to support this view. Robinson and Einarson cite 11 studies in their letter, but not one demonstrates better obstetrical outcomes in SSRI-treated pregnancies. No such study exists. Numerous studies are available that compare depressed pregnant women on SSRIs with those not taking medication and none of them show better pregnancy outcomes in the SSRI group. Surely, if the conventional wisdom was correct—that depression leads to pregnancy complications and treatment improves the depression—then we should see at least a few studies showing better pregnancy outcomes in the antidepressant-treated groups, but we never do. This is dramatically different to, for example, the evidence supporting the use of insulin to improve outcomes in diabetic pregnancies.

We are also concerned that Robinson and Einarson do not adequately address the scientific evidence which can lead to providing