Can assisted reproductive technologies help to offset population ageing?

Sir,

In the challenging paper by Hoorens et al. (2007) which is a condensed version of a Rand Corporation Report by the same authors (Grant et al. 2006), the authors argue that the trend of population ageing as a result of decreasing birth rates and longer life-expectancies is a serious threat for most EU member states. They compare the situation of the UK and Denmark in 2002 with regard to the total fertility rate (TFR, the mean number of children per woman), the age of the mother at childbirth and the number of IVF cycles per million inhabitants. On the basis of the spontaneous and the IVF pregnancy rates, they construct a fertility model and demonstrate that if the access to IVF in the UK were increased to the much higher IVF capacity in Denmark, the TFR in the UK would increase by 0.04. Moreover, if all infertile couples would have access to IVF, the so-called ‘maximum TFR with ART’ (Fig. 1 and Table II) would rise by 0.20 in the UK and 0.17 in Denmark implying enormous rises in IVF capacity. Compared with other policy measures intended to increase national birth rates, these are considerable effects. The authors conclude that IVF and other assisted-reproductive technologies (ART) have the potential to increase birth rates, thereby helping to offset the trend of population ageing.

However, several of the results and conclusions of the study are based on inappropriate definitions and flawed assumptions. In Appendix A of the RAND Report, to which the article and its technical paragraph refer, the fertility definitions are given. Couples are fertile if a spontaneous pregnancy leading to live birth is achieved within 1 year after stopping birth control. In spite of having regular, unprotected intercourse, they do not conceive within that crucial period, they are to be considered as subfertile, which condition is potentially restorable by IVF. However, if IVF appears to be ineffective, the couple is to be categorized as sterile: with this male partner the woman will never conceive. These definitions imply (i) that IVF is indicated for all couples who do not conceive spontaneously within 1 year and (ii) that all couples, who do have a child after IVF, would have been otherwise childless. This view on fertility ignores the overwhelming evidence from the literature about the ability of couples to have a natural conception leading to live birth after 1, 2 or more years of unsuccessfully trying (Tietze, 1950; Leridon, 1977; Collins et al., 1983; Spira, 1986; Wood, 1989; van der Steeg et al., 2007 and many others). For example, about half of all the couples, who do not achieve a natural pregnancy within 1 year after stopping birthcontrol, will still do so during the following year (te Velde et al., 2000; Dunson and Baird, 2004). Applying IVF to all couples who have not become pregnant within 1 year is unnecessarily exposing many of them to the complications and side effects of a potentially risky treatment modality.

The authors do not seem to realize that the demographic advantage of early IVF—a higher TFR—for a considerable part is due to the high incidence of children from twin and triplet pregnancies after IVF (Andersen et al., 2006). Such children have a much higher probability of immaturity or prematurity associated with increased risks of infant mortality and morbidity after delivery and of cognitive problems and long-term handicaps later in life (Helmerhorst et al., 2004; Hille et al., 2007). In their cost–benefit analysis, the authors only include the direct costs of the IVF treatment, neglecting the much higher costs of the complications by premature and immature births, and the treatment-related complications for the mother (Collins, 2002).

In conclusion, we think that IVF is the most important treatment for couples who have no or little chance of conceiving naturally and that all these couples should have the opportunity to have IVF. However, early IVF is only indicated in the minority of couples: those who have a clearly identifiable cause of their infertility. Many couples need more time for realizing a natural pregnancy. Hoorens et al. grossly overestimate the impact of IVF as a policy measure to boost birth rates. If governments would follow their recommendations, this would have serious health consequences for mothers and children.

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Reply: Can assisted reproductive technologies help offset population ageing?

Sir,

We warmly welcome scrutiny of our work and the open debate that it has prompted. However, we believe Te Velde et al. misrepresent our thesis and misstate our definitions and assumptions.

In our exploratory work, we tested the hypothesis that assisted reproductive technologies (ART) could be part of a population policy mix and concluded that ‘ART does have potential to contribute to the total fertility rate (TFR)’ (Grant et al., 2006; Hoorens et al., 2007). In reaching this conclusion, we have repeatedly stressed a number of caveats and limitations to our analysis and the need for further research. Indeed, the RAND Europe report to which Te Velde et al. refer is titled ‘A preliminary assessment of the demographic and economic impact of Assisted Reproductive Technologies’ [our italics]. At no time have we made ‘recommendations’ to government about adopting ART as a part of a population policy as Te Velde et al. claim.

Te Velde et al. dispute two parts of our analysis—the infertility definition and the cost–benefit assumptions. First, we stress that the definition of infertility has no material impact on our central finding that the TFR in the UK would increase by 0.04, if Danish ART practice was adopted. We only used the proportion of women with conception difficulties by age to provide an upper bound estimate on the impact of ART on TFR (0.20 in the UK). We do not, as Te Velde et al. suggest, use a 1 year period of unprotected intercourse as a threshold value for the infertility definition. As explained in our paper, there are intrinsic difficulties with such an estimate.

Unfortunately, the literature does not present a coherent and consistent definition of infertility. In the paper, we showed that there is a significant variation between different estimates of infertility. We agree that conservative definitions should be used in order not to overestimate the impact and recommended that future studies should address this issue in more detail. Therefore, we decided to use an average of the estimates with a 2 year threshold produced by Van Balen et al. (1997), Bongaarts (1982) and Dunson et al. (2004).

We appreciate Te Velde et al.’s comment about the accuracy of our assumption that all couples who do have a child after ART would have been otherwise childless. We acknowledge in our paper the non-negligible probability of spontaneous pregnancy for couples undergoing ART. Evers et al. (1998), for example, found a 12 month cumulative probability of spontaneous pregnancy rate between 2.4% and 6.6% for patients with ‘severe reproductive disorders’ on the waiting list. Nonetheless, a recent paper by Sobotka et al. (2008) using a different methodology resulted in very similar estimates for the ‘net’ impact of assisted reproduction on fertility rates as those resulted from our study. In their analysis, Sobotka et al. do compensate for the probability of spontaneous pregnancy.

It is important to emphasize that our definition of infertility is a classification for the purpose of implementing a forecast model, not a diagnosis. Distinctions must be made somewhere; infertility is spectral, but policy decisions (e.g. ART indications or eligibility) are discrete. Moreover, infertility is distributed both biologically and in terms of outside observers’ estimates. Observed experience (e.g. time-to-pregnancy) may increase the accuracy of infertility estimates, but they remain imperfect—even taking into account, as a clinician would, the frequency and timing of intercourse and other observable factors such as smoking, stress, physical condition, etc. Hence, any rules, including those of Te Velde et al., produce errors.

The discussion of classifications is really a matter of thresholds, and not just diagnostic precision. Thresholds are tied to policy and medical decisions and thus must balance costs and benefits. In addition to natural and imperfectly observable heterogeneity in pair fertility across the population, there is a general drift downward with age. Even without cost considerations, setting a threshold represents what statisticians call a ‘bandit’ problem—a choice under uncertainty where gathering more information (e.g. by undergoing or not undergoing ART) changes both beliefs and the true state of the underlying stochastic process. Moreover, infertility itself (i.e. as distinct from clinicians’ posterior estimates) is multi-dimensional; it includes the infertility of the pair and the individuals, ‘infertility-without ART’, ‘infertility-under-ART’ and even ‘infertility without ART but after prior ART’, etc. The definition(s) we used are meant to establish working clarity,